FALLER, RACHEL E. WILLIAMS. Ph.D. Association between HIV care and the syndemic burden of intravenous drug use, mental health, and HIV stigma. (2022)
Directed by Dr. Jennifer Toller Erausquin. 126 pp.

Initial linkage to and ongoing engagement in HIV medical care among people who inject drugs who are living with HIV (PWID/LWH) are challenging but vital components of ending the HIV epidemic in the United States. However, PWID/LWH are less likely to be engaged in care than those that do not inject drugs, resulting in higher risk of poor health outcomes and HIV transmission. PWID/LWH may have multiple barriers to HIV care, including mental health conditions such as depression and anxiety. Further complicating HIV care among PWID/LWH is the discrimination and stigma they experience. These complex, synergistic relationships between multiple diseases and adverse social conditions, which result in poor health outcomes, can be better understood using syndemic theory. The purpose of this dissertation is to examine the association between HIV care and the syndemic burden of intravenous drug use, mental health, and HIV stigma. Using data from three Southern states participating in the Centers for Disease Control and Prevention's Medical Monitoring Project, the construct validity of measurement models for syndemic burden and HIV care and coverage were tested using confirmatory factor analysis. Each resulting measurement model was included in a structural equation model to assess the association between syndemic burden and HIV care and coverage. Results showed a statistically significant negative correlation between HIV care and coverage and the syndemic burden of intravenous drug use, mental health, and HIV stigma among PLWH. HIV stigma, depression symptoms, and anxiety symptoms were the greatest indicators of syndemic burden, while care retention, ART adherence, and viral suppression were the greatest indicators of HIV care and coverage. In addition to stigma and mental health, this study found female/transgender, less than high school education, younger age, and non-Hispanic Black race/ethnicity were all

associated with higher levels of syndemic burden. A notable outcome from this study was that ever-injecting drugs was not a statistically significant factor for syndemic burden. Since almost 80% of participants reporting ever-injecting drugs did not report injecting in the past year, this result may reflect resiliency and social support associated with being in recovery. Results of this study suggest HIV stigma and mental health could be targets for intervention to improve HIV care outcomes. Future research should identify and assess potential mechanisms driving relationships between syndemic indicators and explore aspects associated with recovery that may reduce syndemic burden or improve HIV care among PWID/LWH.

ASSOCIATION BETWEEN HIV CARE AND THE SYNDEMIC BURDEN OF INTRAVENOUS DRUG USE, MENTAL HEALTH, AND HIV STIGMA

by

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A Dissertation

Submitted to

the Faculty of The Graduate School at

The University of North Carolina at Greensboro

in Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

Greensboro

2022

Approved by

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ACKNOWLEDGEMENTS

First and foremost, I want to thank my amazing committee—Dr. Toller Erausquin, Dr. Tanner, Dr. Nichols, and Dr. Jones—for their guidance and support while I navigated this journey, both academically and personally. I could have never reached this point without your expertise and wisdom.

Furthermore, I could not have completed this study without the wonderful people at the Florida Department of Health, the Georgia Department of Public Health, and the Virginia Department of Health—a special thank you for your support and patience, especially during a pandemic!

I am eternally grateful for the support of my family and friends throughout this journey. To my husband Chris, thank you for listening (even when you had no idea what I was talking about) and not letting me give up. However, I still think you need a better retirement plan than just me. To my parents, Drs. Paul and Katherine Williams, I could never put into words how much your love and support means to me. Thank you for putting this journey in perspective—you were right, at least I did not have to write this up on a typewriter. To Kate, Sherry, Tammy, the Krewe—Gretchen, Kristen, Tiffani, and Mary (keep it spooky!)—and Tailgaters Anonymous (go Canes!) thank you for always being there and cheering me on!

And last, but certainly not least, to my chihuahua Chadwick, thank you for keeping my lap warm during those long days at the computer and reminding me, constantly, to get up and step outside once in a while.

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CHAPTER I: INTRODUCTION

Introduction to Focus of Study

Initial linkage to and ongoing engagement in HIV medical care among people who inject drugs living with HIV (PWID/LWH) are challenging but vital components of the Ending the HIV Epidemic (EHE) plan in the United States (United States Department of Health and Human Services [DHHS], 2019). HIV care engagement increases adherence to antiretroviral therapy (ART), which reduces the amount of virus in the blood (i.e., viral load). PWID/LWH are less likely to be engaged in care than those that do not inject drugs, resulting in higher risk of poor health outcomes and HIV transmission (Dasgupta et al., 2021; Wood et al., 2003, 2009). To reduce this risk, engaging PWID/LWH into care is of extreme importance. One barrier to care engagement in PWID/LWH is mental health conditions, such as depression and anxiety. PWID/LWH have higher rates of depression and anxiety when compared to people living with HIV (PLWH) who do not inject drugs (Cook et al., 2007; Taniguchi et al., 2014). Anxiety and depression, which are often inseparable comorbidities of addiction, reduce self-efficacy and motivation for adhering to ART (Chander et al., 2006). Additionally, relationships between mental health and ART adherence are often affected by gender, with women experiencing greater severity of mental health conditions and lower ART adherence than males (Chander et al., 2009; Ogburn et al., 2019). Mental health is then often worsened by the stigma PWID/LWH face (Cama et al., 2016; von Hippel et al., 2018). These complex relationships between mental health, intravenous drug use (IDU), stigma, and sociodemographic factors constitute a syndemic. The term syndemic is used to describe the complex, synergistic relationships between multiple diseases and adverse social conditions, which result in poor health outcomes (Singer & Clair, 2003). However, using a syndemic approach does not simply explore comorbid conditions.

Rather, syndemic theory recognizes that biological consequences of diseases and multiple behaviors, experiences, and contexts are all interrelated and experienced simultaneously, resulting in unique health outcomes.

The purpose of this dissertation is to examine the associations between HIV care and the syndemic burden of mental health, IDU, and HIV stigma. I will first present a review of the literature (Chapter 2). The review will begin with a brief overview of HIV among PWID and the HIV care continuum. Then, I will review our current knowledge of HIV care engagement among this population and its associations with mental health. Finally, I will summarize the literature on HIV stigma and HIV care engagement among PWID/LWH. The second portion of Chapter 2 will present a summary of my theoretical framework (i.e., syndemic theory). Chapter 3 will describe my conceptual model, the data source (i.e., the Centers for Disease Control and Prevention's [CDC] Medical Monitoring Project [MMP]), and describe the analytic methods for analysis. Results will be presented in two manuscripts (Chapters 4 and 5), followed by a discussion of how the results of each analysis are related (Chapter 6).

Statement of the Problem

PWID/LWH are at high risk for transmitting HIV due to needle sharing. The risk of transmission through needle sharing is likely reduced for those who are virally suppressed, though exact figures for this risk are unknown (CDC, 2022a). Therefore, to reduce the risk of transmission, it is important to engage PWID into the HIV care continuum (i.e., link to and retain in HIV care, adhere to ART, and decrease viral load). HIV care engagement is an effective strategy to increase adherence to ART (Mugavero, 2016). However, IDU is a known barrier to HIV care (Fleishman et al., 2012). This barrier is further complicated by the high prevalence of comorbid mental health conditions in PWID/LWH, such as depression and anxiety. PWID/LWH

have high rates of these conditions due, in part, to discrimination and stigma they experience (Cama et al., 2016; von Hippel et al., 2018). Previous research has established correlations between depression and anxiety, drug use, HIV stigma, HIV care engagement, and ART adherence (Chander et al., 2009; Li et al., 2020; Ogburn et al., 2019; Rao et al., 2012; Rueda et al., 2016; Tucker et al., 2003). However, less is known about the syndemic burden associated with these relationships and if that burden is further associated with HIV care. In addition, little research has specifically included PWID/LWH. The lack of understanding resulting from these gaps in our knowledge leads to interventions that do not adequately address mental health conditions and HIV stigma affecting HIV care among PWID/LWH, which increases the risk of new HIV infections and poor health outcomes.

Significance of the Study

This study will address gaps in current research on HIV care engagement, mental health, and HIV stigma among PWID/LWH by using population representative data which includes PWID/LWH. In addition, this study will address IDU, mental health, and stigma as a syndemic, which is important due to the complex, interactive relationships between these conditions. The overall objective of this study is to examine the relationship between HIV care and the syndemic burden of mental health, IDU, and HIV stigma. To attain the overall objective, I will examine the following three aims:

- Aim 1: Assess the construct validity of a theoretical model of the syndemic burden of mental health, IDU, and HIV stigma
- Aim 2: Assess the construct validity of a theoretical model for HIV care and coverage
- Aim 3: Evaluate the direction and extent of the association between the syndemic burden of mental health, IDU, and HIV stigma and HIV care and coverage

CHAPTER II: REVIEW OF THE LITERATURE

Chapter 2 presents a review of the literature on six areas related to the present study: 1) the HIV epidemic among PWID, 2) the HIV care continuum and the role of HIV treatment in ending the epidemic, 3) the HIV care continuum in PWID, 4) mental health and HIV care, 5) stigma and HIV care, and 6) the use of syndemic theory in HIV research. This chapter provides a description and justification for the focus on mental health and stigma among people who inject drugs and are living with HIV, and for the application of syndemic theory to this population and HIV care outcomes.

First, I describe the current HIV epidemic among PWID in the United States. Next, I provide a brief overview of the HIV care continuum and its relevance for ending the epidemic. I follow by reviewing current research on PWID engagement in each step of the HIV care continuum, including a summary of barriers to care in this population. I then focus on mental health conditions as barriers and how they affect HIV care among PWID. Next, I provide an overview of stigma as a contributor to poor mental health and as a barrier to HIV care. Finally, I provide a description of syndemic theory, its use in HIV research, and how it applies to the current study.

HIV in PWID

Meeting the needs of PWID is of critical importance to ending the HIV epidemic in the U.S. New HIV diagnoses due to IDU have increased in recent years. HIV incidence due to needle sharing can be difficult to estimate due to confounding factors such as unprotected sex; however, CDC estimates that since 2014, the proportion of new HIV diagnoses attributable to IDU increased 9% (CDC, 2020c). As of 2018, HIV incidence among PWID was greatest among whites (44.9% of new HIV infections among PWID) and men (57.5%) (CDC, 2020a). The

demographics of incident HIV among PWID suggest the recent increase in HIV attributable to IDU may be due to the ongoing opioid epidemic and particularly the increase in injection of heroin, which has affected white men at higher rates than other races/genders (Hodder et al., 2021; Jones et al., 2015).

The high risk of contracting HIV among PWID is primarily due to needle sharing—a direct route of HIV transmission through needles contaminated with blood. According to CDC, a person using a needle previously used by someone with HIV has a one in 160 chance of contracting the virus with each exposure (CDC, 2019b). However, multiple exposures increase risk of infection over time. PWID are significantly more likely to be HIV-positive when they have frequent exposures to shared needles, i.e., if they have been using for a long period of time, injected more than one type of drug, and/or injected drugs with strangers (Rondinelli et al., 2009). Several studies have identified risk factors associated with the practice of needle sharing among PWID. These factors include mental health conditions, homelessness, low social support, polydrug use, incarceration, and injecting with multiple people (Conner et al., 2008; Edelman et al., 2014; Harrell et al., 2012; Metsch et al., 2007; Mizuno et al., 2015; Wagner et al., 2009). Having more than one of these factors increases the likelihood of needle sharing, and therefore risk of contracting HIV (Mizuno et al., 2015).

The increase in the proportion of HIV diagnoses due to IDU may not only be because of the opioid epidemic, but also lower access to HIV prevention and treatment strategies for PWID when compared to other groups (e.g., condoms for men who have sex with men [MSM]). For example, while evidence shows syringe exchange programs and opioid replacement therapy are effective at preventing HIV transmission in PWID, these methods are highly regulated and stigmatized (Dawson et al., 2018; Degenhardt et al., 2010; Edelman et al., 2014; Nadelmann &

LaSalle, 2017; Vearrier, 2019; Zampini, 2018). This regulation and stigma results in reduced access to prevention methods and therefore increased risk of transmission (Hodder et al., 2021).

A somewhat less regulated, though still stigmatized, method for preventing HIV transmission is through HIV medical treatment of PLWH. HIV treatment reduces viral loads and therefore likely reduces the risk of transmitting the virus to others through needle sharing, though exact figures on this risk reduction are unknown (CDC, 2022a). Treatment as prevention is one of the four key strategies of U.S. DHHS's EHE initiative, which aims to reduce transmission of HIV in the U.S. by 90% before 2030 (U.S. DHHS, 2021a). In addition, treatment as prevention is a key factor in the Joint United Nations Programme on HIV/AIDS (UNAIDS) 2025 AIDS Targets, which aims for 95% of those infected knowing their status, 95% of PLWH receiving ART, and 95% of those on ART reaching viral suppression before 2030 (UNAIDS, 2020). Its inclusion as a major component of each of these initiatives emphasizes the importance of HIV treatment, not only for improving the health of PLWH, but also as a prevention strategy.

The HIV Care Continuum

Broadly, the treatment pathway for PLWH is known as the HIV care continuum (Mugavero, 2016). It typically consists of four steps: linkage to care, retention in care, ART receipt and adherence, and viral suppression (see Figure 1 below). The first step of the continuum, linkage to care, is ideally completed within 30 days of diagnosis. This linkage ensures PLWH have a regular health care provider knowledgeable about HIV treatment; connecting PLWH to care may be performed by a case manager or diagnosing medical professional. After being linked to a HIV care provider, the second step of the HIV care continuum is retaining the patient in care. Retention in care is defined as visiting a medical professional at least once every six months for HIV-related primary care (AIDSinfo, 2014).

These visits are essential for ensuring patients' HIV treatment is working and, if not, adjusting their treatment.

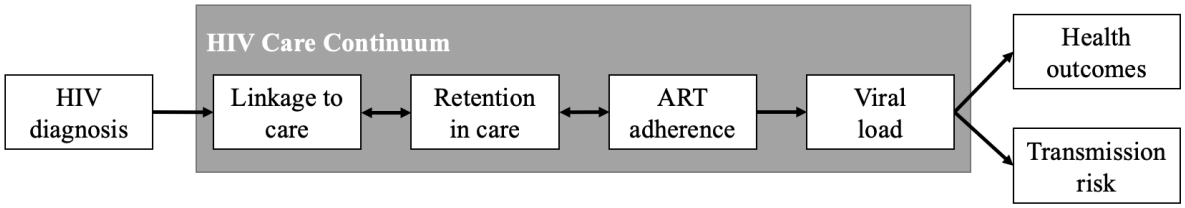
Treatment for PLWH is known as ART (sometimes called highly-active ART [HAART]), and comprises the third step in the HIV care continuum. This step includes both receiving ART (i.e., being prescribed ART by a physician) and ART adherence (i.e., continuing to take ART as prescribed). ART medications work by reducing the ability for HIV to replicate, which reduces the viral load in the blood. However, ART must be used consistently to achieve viral suppression—an adherence rate of between 82% to 95% is needed for viral suppression (Byrd et al., 2019). Most modern ART requires one daily dose. However, PLWH may experience barriers to ART adherence. For instance, patients may lack access to health care, experience negative side effects, or forget doses due to changes in their routine (CDC, 2020b). Missing doses of ART can result in higher viral loads, increased risk of opportunistic infections, and increased risk for antiviral resistance (HIV.gov, 2022).

While any reduction in viral load is important, ideally a person using ART as prescribed will become virally suppressed. Viral suppression, defined clinically as <200 copies of HIV/mL of blood, is essential for preventing opportunistic infections and reducing the risk of HIV transmission. The lower a person's viral load, the less likely they are to infect others—if a person's viral load is undetectable (i.e., the virus is not detectable using conventional blood tests), they *cannot* transmit the virus to others through sex (CDC, 2018).

It is important to note that PLWH may not follow these steps sequentially. Some patients may move back and forth between steps. For instance, if a PLWH who is retained in care moves to another state, they will need to be re-linked into care with a closer physician. This example

demonstrates how the HIV care continuum is more like a cascade, with PLWH falling into higher or lower levels of care engagement (Mugavero, 2016).

Figure 1. The HIV Care Continuum



Note. The HIV care continuum begins with linkage to care after an HIV diagnosis. The goal is to retain patients in care to improve ART adherence. ART adherence decreases viral load, leading to better health outcomes and less risk of transmission. The double-sided arrows represent the potential for people living with HIV to move back and forth between linkage to care, retention in care, and ART adherence, demonstrating that the continuum is more of a cascade from higher to lower levels of care engagement. ART = antiretroviral therapy. Adapted from Mugavero (2016).

The HIV Care Continuum in PWID/LWH

As stated above, the HIV care continuum is essential for lowering the risk of transmission and improving health outcomes among PLWH by lowering viral loads. However, once diagnosed with HIV, PWID are less likely to be engaged at all stages of the HIV care continuum than those that do not inject drugs. Therefore, PWID/LWH are at risk for poor health outcomes and greater risk of transmission to others.

Linkage to and Retention in HIV Care in PWID/LWH

PWID/LWH are less likely to be linked and retained in HIV care than other PLWH. For instance, an analysis of data from the HIV Research Network compared three measures of HIV care engagement between PWID/LWH and MSM living with HIV. Patients (n = 22,984) were considered linked to, but not retained in, care if the period between their first and last outpatient visit on record was more than six months. Retention in care was measured using two different definitions: 1) two outpatient visits each year at least 91 days apart or 2) no loss to follow-up greater than 12 months. Results of logistic regression analysis showed the odds PWID were

linked to, but not retained in, care were 49% less than those in MSM (adjusted odds ratio [AOR] = 0.51; 95% confidence interval [CI] = 0.44, 0.59; $p < 0.001$). PWID also had significantly lower odds of having no loss to follow-up greater than 12 months (AOR = 0.66; 95% CI = 0.57, 0.77; $p < 0.001$). However, when retention was measured as two outpatient visits each year, there were no significant differences between PWID and MSM (AOR = 0.86; 95% CI = 0.70, 1.06; $p > 0.05$) (Fleishman et al., 2012). The difference between retention outcomes may be due to the way they are measured as PWID who visit an HIV care provider every six months would not be lost to follow-up for longer than 12 months.

Another study analyzed longitudinal data from the AIDS Linked to the Intravenous Experience (ALIVE) study to assess differences in care engagement among PWID/LWH (n = 790). Linkage to care was defined as attending at least one study visit over the course of the study. Retention in care was defined as either partial retention (having a six-month interval with no HIV care) and full retention (attending two visits each year six months apart). Overall, 93.6%, 63.2%, and 30.5% of PWID were linked to care, partially retained in care, and fully retained in care, respectively. Of those never linked to care, 74% had injected a drug in the past six months while only 51.4% and 50.8% of PWID partially and fully retained in care had ($p < 0.01$). PWID who had injected drugs in the past six months had greater odds of their last HIV care visit having occurred more than six months ago, compared with those who had not injected a drug in the past six months (AOR = 1.25; 95% CI = 1.06-1.49) (Westergaard et al., 2013).

Another longitudinal study on PLWH receiving HIV care at Johns Hopkins (The Johns Hopkins HIV Clinical Cohort [JHHCC]) compared proportions of patients retained in HIV care, defined as at least two HIV care visits >90 days apart over one year, between PWID/LWH (n = 1,104) and PLWH not injecting drugs (n = 1,922). Results showed that while the proportion of

PWID/LWH retained in care increased over time (from 68.4% in 2001 to 82.2% in 2012), the proportions were still lower than in PLWH who did not inject drugs (except for in 2012). When adjusted for baseline demographics and clinical status a similar trend occurred, with PWID/LWH having a significantly lower probability of being retained in care than those not injecting drugs from 2001 to 2010 (Lesko et al., 2017). These studies show PWID/LWH are less likely than PLWH who do not inject drugs to be linked to and retained in care. It is therefore not surprising that PWID/LWH are also less likely to receive and adhere to ART than PLWH who do not inject drugs, as I discuss in the next section.

ART Receipt and Adherence in PWID/LWH

The low rates of linkage and retention in care among PWID/LWH lead to low rates of ART receipt and adherence in this population. For instance, Himelhoch et al. (2007) found odds of PWID/LWH receiving a prescription for ART were lower when compared to those who do not inject drugs (AOR = 0.64; 95% CI = 0.58, 0.85; $p < 0.05$). Similarly, a review by Chander et al. (2006) found studies on primary care sites in the United States, the Swiss Cohort, and the French MANIF cohort all demonstrated odds of PWID/LWH being prescribed or receiving ART were lower than those of people who do not inject drugs. More recent studies show similar results. McGowan et al. (2011) assessed ART receipt (defined as ever receiving ART for at least seven continuous days) among PWID/LWH in two cohorts of patients, one in Nashville, TN (n = 1,745), and another in Baltimore, MD (n = 1,977). Those with a history of IDU had significantly lower odds of receiving ART than those without a history of IDU in both cohorts (Nashville cohort: AOR = 0.61; 95% CI = 0.45, 0.84; $p = 0.003$; Baltimore cohort: AOR = 0.58; 95% CI = 0.46, 0.73; $p < 0.001$) (McGowan et al., 2011).

Differences have also been identified among those *currently* and *formerly* injecting drugs. For instance, among those currently injecting drugs, a meta-analysis of six studies on PWID/LWH in the U.S. (n = 608) found those currently injecting drugs (i.e., injecting within the past 30 days) had significantly lower odds of receiving ART over the past 30 days than those not currently injecting (AOR = 0.51; 95% CI = 0.36, 0.72; $p < 0.001$) (Wagman et al., 2020). This disparity may be due to provider biases related to drug use. Westergaard et al. (2012) conducted a survey of HIV care providers in the U.S. and Canada and found that while only 24.2% of providers would defer prescribing ART to those formerly injecting drugs, over half (52.4%) would defer ART in those injecting drugs daily. It should be noted that all these studies on ART receipt were conducted in PWID/LWH engaged in the medical system. Since ART requires the prescription of a healthcare provider, ART receipt is certainly lower for PWID/LWH who are not engaged in the medical system.

Unfortunately, data suggest that even when PWID/LWH are prescribed ART, they have low levels of medication adherence. For instance, a study on PWID/LWH recruited for an HIV prevention intervention (n = 1,052) found 43.6% were not currently taking ART and 25.3% of those taking ART were <90% adherent (Mizuno et al., 2015). These lower rates in ART adherence among PWID/LWH are also seen over time. A longitudinal study by Lesko et al. (2017), which defined using ART as at least one prescription for ART for at least 30 days during the year, compared ART use trends between PWID/LWH and PLWH not injecting drugs between 2001 and 2012. Results showed an increase in the proportion of PWID/LWH on ART over the study period (from 45.5% in 2001 to 76.3% in 2012), but these rates were consistently lower than among PLWH not injecting drugs (62.4% to 77.1%). However, when only including those retained in care (i.e., at least two HIV care visits >90 days apart over one year), there were

no significant differences in ART use between PWID/LWH and PLWH not injecting drugs (Relative Risk [RR] of using ART = 0.94; 95% CI = 0.88, 1.01) (Lesko et al., 2017). Another longitudinal analysis used data from three longitudinal cohorts of PLWH and compared ART utilization trends in PWID/LWH (n = 843) and those not injecting drugs (n = 1,423). PWID had a shorter period between initiating and discontinuing ART than those not injecting drugs (median = 1.1 vs. 2.5 years, respectively). In addition, PWID/LWH had an overall higher risk of discontinuing ART than PLWH not injecting drugs (adjusted Relative Hazard [aRH] = 1.24; 95% CI = 1.03, 1.48). The study further assessed differences between current and former PWID and found those currently injecting drugs were more likely to discontinue ART than those never injecting drugs (aRH = 1.65; 95% CI = 1.23, 2.22); however, no significant difference was seen between those formerly and never injecting drugs (aRH = 1.16, 95% CI = 0.96, 1.41) (Morris et al., 2007). Collectively, these studies show that PWID/LWH have less than ideal rates of ART adherence, especially in those *currently* injecting drugs.

Viral Suppression in PWID/LWH

As a result of low ART receipt and adherence, PWID/LWH have low rates of viral suppression. For instance, Mizuno et al. (2015) analyzed baseline characteristics of a convenience sample of PWID/LWH from four U.S. cities (n = 1,052). Only 19.6% of the sample, which consisted of mostly Black (65.4%), low income (<$5,000/year; 53.3%), and men (63.3%), were virally suppressed (defined as <400 copies/mL) (Mizuno et al., 2015). This percentage is significantly lower than CDC's estimated 80% rate of viral suppression among PLWH in the United States (CDC, 2018). Those currently injecting drugs are also less likely to be ART adherent than those who no longer inject drugs. For instance, a meta-analysis by Wagman et al. (2020) found that PLWH who currently inject drugs (i.e., injected drugs in the past 30-days) had

44% lower odds of viral suppression than PLWH who formerly injected drugs (AOR = 0.56; 95% CI = 0.39, 0.80; $p = 0.002$). PWID/LWH are also less likely to maintain viral suppression. A longitudinal study of PWID/LWH found that even though a majority achieved viral suppression at some point during the 8.7-year follow-up (85.4%), consistent viral suppression, defined as viral suppression at all care visits over the study period, was only seen in 10.2% of participants (Westergaard et al., 2013). Another longitudinal study found similar results, with consistently lower rates of viral suppression (<400 copies/mL) among PWID/LWH than PLWH who do not inject drugs across the 12-year study period (28.0% to 69.1% and 41.7% to 71.0%, respectively). However, when those not taking ART were excluded from the analysis, the viral suppression rate was not significantly different between the two groups for all years except 2004 (Lesko et al., 2017). This result may indicate that the disparities between PWID/LWH and PLWH not injecting drugs is due to lack of ART receipt and adherence.

Barriers to the HIV Care Continuum in PWID/LWH

Research has identified many factors acting as barriers to engagement in the HIV care continuum among PWID/LWH. These factors include sociodemographic characteristics, personal attitudes and beliefs, difficult life circumstances, and comorbid health conditions. For instance, one study among PWID/LWH (n = 1,052) found polydrug use (OR = 1.59) and homelessness (OR = 2.39) are barriers to ART adherence (Mizuno et al., 2015). A recent systematic review by Bazzi et al. (2019) also identified incarceration and history of sexual abuse as factors for non-adherence among PWID/LWH. Other factors associated with non-adherence among PWID/LWH included younger age, female sex, lower levels of education, and minority race/ethnicity. Finally, health-related factors associated with non-adherence included poor physical health, health and ART-related beliefs, and risk behaviors such as high-risk sexual

behaviors (e.g., sex work) and needle sharing (Bazzi et al., 2019). Viral suppression among PWID/LWH also depends on other risk factors. Among PWID/LWH, polydrug use, low social support, and homelessness are associated with lower likelihood of viral suppression (Mizuno et al., 2015).

In addition to these factors, several studies have identified mental health conditions as being associated with poor ART adherence and low rates of viral suppression among PWID (Bazzi et al., 2019; Himelhoch et al., 2007; Mizuno et al., 2015; Robinson & Knowlton, 2016; Waldrop-Valverde & Valverde, 2005). The association of mental health with low ART adherence and lack of viral suppression among PWID/LWH is particularly concerning due to the high prevalence of comorbid mental health conditions in this population.

Mental Health Conditions in PWID/LWH

Intravenous drug use and mental health are highly associated. Research has shown higher rates of depression, anxiety, suicidal ideation/attempts, bipolar disorder, obsessive compulsive disorder (OCD), post-traumatic stress disorder (PTSD), and personality disorders in PWID compared to people who do not inject drugs (Colledge et al., 2020; Conner et al., 2008; Jones et al., 2010; Kidorf et al., 2018; Mackesy-Amiti et al., 2012; Nowotny et al., 2017). Not surprisingly, similar associations are seen with mental health in PWID/LWH. For instance, Jones et al. (2010) compared various psychosocial measurement scores (i.e., Beck Depression Inventory, Profile of Mood States, Structured Interview Guide for the Hamilton Anxiety and Depression) of PWID/LWH, PWID, and people who do not inject drugs and are not living with HIV (n = 416). PWID/LWH and PWID had significantly higher levels of depression and anxiety compared to people who do not inject drugs and are not living with HIV. However, PWID/LWH had lower levels of depression and anxiety than PWID. The authors note this difference could be

due to greater access to health care for PWID/LWH due to their HIV status (Jones et al., 2010). However, another study, which analyzed similar population groups (n = 61), found PWID/LWH had significantly higher levels of depression (Center for Epidemiologic Studies Depression Scale [CES-D] = 23.27) than PWID (15.24), PLWH (15.33), and people who do not inject drugs who are not living with HIV (19.47; all $p < 0.05$) (Wisniewski et al., 2005). Both these studies show significant differences in mental health between PWID/LWH and those not injecting drugs or living with HIV.

The burden of mental health conditions among PWID/LWH is particularly experienced by women. For instance, mental health conditions such as depression and anxiety are more prevalent among women living with HIV who inject drugs than men living with HIV who inject drugs (Genberg et al., 2019; Robinson & Knowlton, 2016; Wisniewski et al., 2005). One study found women living with HIV who injected drugs had the highest proportion of those with depression (83%) when compared to men and women who inject drugs and are not living with HIV, who are living with HIV but do not inject drugs, and who were in neither category (other percentages not reported) (Wisniewski et al., 2005). Another study of Black PWID/LWH found lower proportions of women with at least one mental health condition (68.2%). However, this study found women had a higher proportion of one or two mental health condition diagnoses (46.6%) and three or more diagnoses (31.8%) when compared to men (38.3% and 23.4%, respectively) (Robinson & Knowlton, 2016). Women were also found to have higher rates of depression. An analysis of data from the ALIVE study (n = 1,544) found that overall, 39.6% of PWID/LWH experienced depression symptoms as measured by a CES-D score of at least 16. However, over half (51.5%) of female PWID/LWH experienced depressive symptoms (Genberg et al., 2019). These studies suggest men and women who inject drugs and are living with HIV

have different combinations of symptoms and different diagnosis rates of mental health conditions. Therefore, if we want to fully understand the relationships between IDU and mental health among PWID/LWH, we need to ensure gender is considered as a factor.

Causal Linkage of Mental Health Conditions and IDU

While it is clear mental health conditions and IDU are highly associated, it is less clear if IDU causes mental health conditions or if mental health conditions lead to IDU. The answer to this problem is likely cyclical—mental health conditions can lead to IDU, and IDU can lead to mental health conditions. For example, a longitudinal study found those who stopped injecting drugs during the study period were significantly less likely to experience depressive symptoms (CES-D ≤16) after one year (AOR ± standard error [SE] = 0.40 ± 0.35; $p < 0.01$). No significant change in depressive symptoms was seen in those continuing to inject drugs after one year (AOR ± SE = 1.20 ± 0.29; $p > 0.05$) (Knowlton et al., 2001). This result supports the notion that IDU may cause or exacerbate mental health conditions.

Other studies support the causal link between drug use and subsequent mental health conditions (Bushnell et al., 2019; Reddon et al., 2018). In a retrospective cohort study of adolescents (ages 10-17 years; n = 1,452,972), Bushnell et al. (2019) found 2.9-4.0% of those diagnosed with an anxiety disorder at baseline had a substance use disorder diagnosis after two years compared to 1.1-1.6% of those without an anxiety disorder at baseline. Another study (conducted in Canada) found the incidence of any mental health condition diagnosis among PWID (n = 923) was 4.29 per 100 person years (Reddon et al., 2018). Depression was the most frequently reported incident mental health condition (incidence density = 2.81 per 100 person years), followed by anxiety (1.10) and PTSD (0.29). Factors significantly associated with incident mental health conditions among PWID were being female (adjusted hazard ratio [AHR]

= 1.74; $p < 0.001$), having a non-fatal overdose (AHR = 2.33; $p = 0.002$), using community health services (AHR = 1.53; $p = 0.038$), receiving drug or alcohol addiction treatment (AHR = 1.68; $p = 0.001$), and experiencing violence (AHR = 1.60; $p = 0.011$) (Reddon et al., 2018). This study shows IDU is a precursor to various mental health conditions and that factors associated with incident mental health conditions among PWID are complex.

While the above studies suggest *IDU leads to mental health conditions*, other studies have shown *mental health conditions are a cause for drug use*. For example, Swendsen et al. (2010) used data from the National Comorbidity Survey (NCS) and the NCS-2 follow-up study to assess incident drug use in those with various mental health conditions compared to those without these conditions at baseline. Results showed that during the 10-year follow-up period, those with any mood disorder (AOR = 1.7), any anxiety disorder (AOR = 2.3), or any disruptive behavior disorder (AOR = 2.7) at baseline had significantly higher odds of initiating illicit drug use than those without these conditions at baseline (all $p < 0.05$) (Swendsen et al., 2010).

The conflicting evidence in the literature highlights the difficulty in separating drug use and mental health. However, it also indicates the need for more research on mental health and IDU to improve the understanding of the interrelationships between these phenomena.

Mental Health and HIV Care Engagement in PWID/LWH

Despite high rates of mental health conditions among PWID/LWH, little research has been conducted on effects of mental health on the HIV care continuum among this population.

Mental Health Conditions, IDU, and ART Use and Adherence

Some research suggests that depression, anxiety, and psychological distress are associated with ART use and non-adherence among PWID/LWH (Bazzi et al., 2019; Mizuno et al., 2015; Waldrop-Valverde & Valverde, 2005). For instance, one study among PWID/LWH (n

= 58) found those with greater levels of depression had significantly lower odds of treatment adherence (AOR = 0.92; 95% CI = 0.86, 0.99; $p = 0.02$) (Waldrop-Valverde & Valverde, 2005).

Another study assessed the relationships between appearance concerns related to side effects of ART (e.g., weight gain or loss, hair loss, etc.), depression (measured using the Clinical Global Impression [CGI] score), and ART adherence (measured using electronic pill caps as not taking a dose of ART within two hours of target time) among PWID/LWH receiving treatment for opioid use disorder (n = 89). Results indicated that depression severity was significantly associated with ART non-adherence (direct effect = 3.3; 95% CI = 0.8, 5.8; $p = 0.01$). Further, the relationship between appearance concerns and ART non-adherence was mediated by depression severity (indirect effect = 1.02; 95% CI = 0.21, 2.1), indicating that depression resulting from HIV-related causes negatively affects ART adherence (Blashill et al., 2014). This study demonstrates the relationships between ever using drugs, mental health, and impacts of living with HIV can directly affect ART adherence.

Finally, an analysis of data from the Intervention for Seropositive Injection Drug Users - Research and Evaluation (INSPIRE) study assessed the relationship between the number of psychosocial factors (polydrug use, childhood abuse, psychological distress, low social support, homelessness, and incarceration) and ART adherence. Results showed no significant association between psychological distress alone and not currently taking ART. However, when interacting with other psychosocial factors, results showed an additive trend: those with one (AOR = 2.03), two (AOR = 2.07), three (AOR = 2.79), or four to six (AOR = 2.47) psychosocial problems had significantly higher odds of not currently taking ART when compared to those with no problems (all $p < 0.01$). For those taking ART, those with three (AOR = 2.34) or four to six (AOR = 2.56) problems had significantly higher odds of non-adherence (all $p < 0.05$) (Mizuno et al., 2015).

While results for retention in care (i.e., at least one HIV care visit in the past six months) were not significant for PWID/LWH experiencing psychological distress or any other number of psychosocial problems, this could be a result of sample bias related to already being engaged with the research study (Mizuno et al., 2015). This study highlights the interactive effect of mental health with other psychosocial factors and that these interactions are associated with poor ART adherence.

Mental Health, IDU, and Viral Suppression

Rates of viral suppression among PWID/LWH are also low. One study that used hospital visit data of PLWH (n = 5,119) found that in PWID with serious mental health conditions, viral suppression (≤400 copies/mL) was achieved by only 33.3% compared to 43.7% in those without serious mental health conditions or IDU (Himelhoch et al., 2007). Another analysis of the INSPIRE study supports this result. Mizuno et al. (2015) found PWID/LWH who experienced psychological distress in the past week had significantly higher odds of viral load ≥400 copies/mL (OR = 1.46; 95% CI = 1.04, 2.03; $p < 0.05$). In addition, those experiencing four to six psychosocial problems had significantly greater odds of having a detectable viral load (AOR = 2.24; 95% CI = 1.18, 4.27; $p < 0.05$) (Mizuno et al., 2015). However, Robinson & Knowlton (2016) found contradicting results when analyzing data from a sample of Black PWID/LWH enrolled in the Being Active and Connected (BEACON) study (n = 383). Men with one or two diagnosed mental health conditions were significantly more likely have an undetectable viral load (≤40 copies/mL) than those with no diagnosed mental health conditions (adjusted incidence rate ratio [AIR] = 1.28; 95% CI = 1.000, 1.63; $p < 0.05$). There were no significant effects seen in men with three or more mental health conditions or among women, but this result may be due to confounding factors such as sample bias due to the volunteer nature of the sample or

likelihood to seek treatment (i.e., those receiving medical care are more likely to seek treatment for other conditions) (Robinson & Knowlton, 2016).

As the studies described above indicate, mental health conditions are not only prevalent among PWID/LWH, but also a barrier to HIV care. But PWID/LWH have high rates of mental health conditions due, in part, to discrimination and stigma they experience (Cama et al., 2016; von Hippel et al., 2018). Therefore, stigma is important to consider when discussing mental health among PWID/LWH.

Stigma

In this section, I first provide an overview of the concept of stigma. Then, I discuss HIV-related stigma and its effects on HIV care engagement. Next, I describe drug use-related stigma, how it intersects with HIV-related stigma, and their compounded effects on HIV care engagement. Finally, I discuss the consequences of stigma on the mental health of PLWH.

Stigma Overview

Stigma is any belief which results in either the perception of or actual loss of status or social standing at the individual or structural level (Phelan et al., 2014). An individual may experience stigma as a result of interactions with others or negative self-perception. For instance, a PLWH may experience stigma if a person they confide their status in reacts to their diagnosis with disgust. This experienced stigma may also become internalized, i.e., a PLWH may come to feel disgusted with himself/herself/themselves. Other factors at an individual level that can affect the stigma a person experiences include disease characteristics (e.g., contagiousness, visibility), personal characteristics (e.g., age, class), and simply being aware that a stereotype or stigma exists (Pescosolido & Martin, 2015).

In addition to individual-level stigma, stigma can also occur at a much broader, societal level. This broader level of stigma, or structural stigma, is stigma occurring at a societal or cultural level that results in discrimination or oppression of the stigmatized group (Hatzenbuehler, 2018). Structural stigma is often a result of misinformation and fear, threats to privilege and power, and/or existing societal ideals. It is enforced primarily through social norms, which can be driven by a multitude of factors. These factors include national context (e.g., economy, history, health care system), the media (e.g., exposure, genre), and social networks (e.g., size, power and privileges of those within the network) (Pescosolido & Martin, 2015). In addition, stigma can be driven by moral experience, defined by Yang et al. (2007) as "what is most at stake for actors in a local social world" (Yang et al., 2007, p. 1525). Thus, stigma is a response to potential threats to people's ideals and daily existence. For instance, stigma related to HIV is a result of the social moralization of how the virus is transmitted (e.g., through unprotected sex or needle sharing). This moralization contributes to the idea that those infected are somehow corrupt and therefore "deserve" the disease as punishment (Chambers et al., 2015; Hutchinson & Dhairyawan, 2017; Yang et al., 2007). The cultural pervasiveness of this idea, along with other forms of stigma related to sexual orientation, is exemplified in HIV-related laws and policies. For example, some states have laws specifying that a PLWH must disclose his/her/their status to any sexual partner—failing to do so can result in a misdemeanor or felony charge. Although many diseases can be transmitted through unprotected sex (e.g., genital herpes, chlamydia, etc.), HIV is often a target of these criminalization policies due to its associated stigma.

Stigma results in social stratification, with stigmatized groups "ranking lower" in social hierarchy than un-stigmatized groups. Social stratification occurs when an individual or group is

ranked based on how they or others perceive their value (Phelan et al., 2014). For example, a medical provider who stigmatizes HIV may think a patient with liver failure and HIV is less deserving of a liver transplant than someone who is not infected, devaluing the life of the PLWH. According to status characteristics theory, this perceived value is a result of several processes. First, a label is created based on a characteristic deemed important based on contextual relevance or difference from the status quo. Then, each label is linked to an expected outcome. These expected outcomes are based on multiple factors, including cultural norms, stereotypes, politics, and level of privilege or power (Phelan et al., 2014). These expected outcomes are then ranked based on contribution to a group or society or as a way to create separation, i.e., "us" vs. "them" (Phelan et al., 2014). In essence, social stratification due to stigma results from labeling and ranking of preconceived characteristics of an individual or group. This stratification results in the desire to limit interaction with those deemed to have a "lower" value, or social distancing. Likewise, some stigmatized individuals may distance themselves or disengage from groups that discriminate against them or groups that they feel "lower" than due to internalized stigma (Pescosolido & Martin, 2015).

Social stratification is often perpetuated into social distancing by those with "higher" ranking using stigma as a form of power and control. This occurrence, called stigma power, occurs when stigma is used to keep people "in," "away," or "down" (Link & Phelan, 2014). Stigma power enforces social norms (keeping people "in"), excludes those failing to meet these norms or other status quos (keeping people "away"), or exploits or dominates others (keeping people "down") (Link & Phelan, 2014). For instance, people with a mental health condition may be stigmatized in an attempt to change their behavior to be more "normal," or to keep them "in."

If the behavior is more outlandish, for instance in the case of psychosis, they may be stigmatized to keep them "away" or "down" (Link & Phelan, 2014).

HIV-Related Stigma, HIV Care Engagement, & Medication Adherence

The cycle of stigma, social stratification, and stigma power has serious consequences for the health of individuals due to resulting inequality. One consequence is a reduction in HIV care engagement. For instance, Kalichman et al. (2020) conducted a study of PLWH at a clinic in Georgia (n = 251) to assess the cumulative effect of stigma on HIV care engagement. Cumulative stigma was measured by totaling the scores of the HIV Stigma Mechanisms scale conducted each month over the course of a year. Participants were interviewed each month and asked to complete an adaptation of the HIV Stigma Mechanisms scale. Medical chart reviews were conducted to assess retention in care (no missed appointments in the past six months). Results showed cumulative stigma had a significant association with lower care retention (Wald's $\chi^2 = 11.8$; $p < 0.001$) (Kalichman et al., 2020). A study by Rice et al. (2017) found similar results for HIV care engagement. Among PLWH attending a clinic (n = 196), internalized HIV stigma was significantly negatively associated with HIV care visit adherence ($\beta = -0.04$, $p = 0.04$). In addition, internalized HIV stigma was also significantly negatively associated with ART adherence ($\beta = -0.67$; $p < 0.05$) (Rice et al., 2017). In fact, many studies have found this association between HIV stigma and low ART adherence. A meta-analysis by Rueda et al. (2016) found that among studies which controlled for potential confounders, those with higher levels of stigma were less likely to adhere to ART (OR = 0.68; 95% CI = 0.53, 0.87; $p = 0.002$). In addition, a systematic review by Sweeney & Vanable (2016) found similar results. A majority (32 of 37) of the studies identified in the review found stigma was associated with lower ART adherence.

Intersecting Stigmas: HIV and Drug Use

Drug use, like HIV, is highly stigmatized. People who use drugs experience discrimination, alienation, and perceive being devalued by others (Ahern et al., 2007). This stigmatization is the result of many factors, including social norms, stereotypes of those addicted to drugs, and the criminalization of drug use (Ahern et al., 2007; Biancarelli et al., 2019; Hatzenbuehler, 2018). As with HIV stigma, drug use stigma is associated with lower use of health care services (Biancarelli et al., 2019; Muncan et al., 2020). This lower rate of health care utilization is likely because stigma can make people who use drugs uncomfortable seeing a health care provider. For instance, multiple studies have described negative experiences with health care providers among PWID, including name calling, mistreatment, and dehumanization (Biancarelli et al., 2019; Muncan et al., 2020). Many PWID do not feel their health concerns are taken seriously, especially regarding pain since many providers assume they are seeking opioids. Some PWID also report feeling uncomfortable after recognizing subtle behavior changes in their providers after disclosing their drug use (Biancarelli et al., 2019; Muncan et al., 2020).

As I have presented above, HIV and drug use stigma are powerful influences on the health of both PLWH and PWID. However, for PWID/LWH, the presence of both HIV and drug use stigmas creates a complex interaction, which can result in poorer health outcomes than when each stigma is experienced alone. However, it is important to understand that the intersection of multiple stigmas is not necessarily additive. Rather, intersecting stigmas are affected "both by views of how severely a given identity deviates from accepted social norms and the extent to which 'victim blaming' is associated with each identity" (Turan et al., 2019b, p. 3).

Though the effects of intersectional stigma are not always or exclusively additive, research has indicated higher levels of stigma among those with multiple stigmas than among

those experiencing fewer stigmas. For instance, a study on Russian PWID/LWH found an interaction effect of HIV stigma and drug use stigma on number of common health symptoms, but not on overall health status (Calabrese et al., 2016). A qualitative study found Vietnamese PWID/LWH felt their level of stigma experienced in their communities and from family members increased once they were diagnosed with HIV. To avoid the increased stigma associated with using drugs and living with HIV, some PWID/LWH refused to disclose their HIV status with family members. Others reported increased support from their families once they disclosed their HIV status (Rudolph et al., 2012). Another study on Vietnamese PWID/LWH found similar experiences with stigma from community, family, and health care providers. Participants were afraid to disclose their HIV and drug use status to family members. In addition, it was sometimes difficult to separate HIV stigma from drug use stigma experienced by participants in the community. For instance, one participant described hearing a neighbor say to their family that if they were not using drugs, then they would never have been diagnosed with HIV. Others described health care workers treating them poorly after learning about their drug use and HIV status (Do et al., 2021). These studies highlight the complexities of multiple stigmas and how their effects are not simply additive. However, although these studies provide important evidence for intersecting stigmas, it should be noted they may not be generalizable to the U.S., since they were conducted in countries with different cultures and contexts.

Intersecting Stigmas and HIV Care Engagement

Based on the stigma they experience from family, friends, the community, and health providers, it is not surprising that intersecting stigmas in PWID/LWH can impact HIV care engagement. PWID/LWH report experiencing poor treatment by HIV medical providers due to current or previous drug use (Gwadz et al., 2016, 2021; Koester et al., 2019). These negative

experiences result in nondisclosure of drug use to their HIV providers or not going to see providers at all (Gwadz et al., 2016; Koester et al., 2019). However, avoiding HIV care can contribute to internalized stigma, since they may be seen as or feel like a "bad patient," resulting in feelings of shame (Gwadz et al., 2016; Koester et al., 2019). This feeling of shame is an emotional response to stigma, whether internalized (i.e., not meeting one's own expectations of self) or externalized (not meeting expectations of others) (Hutchinson & Dhairyawan, 2017).

In addition to negative experiences with HIV providers, PWID/LWH may feel socially isolated due to the stigmas associated with living with HIV and using drugs. These stigmas are two of many barriers to ART adherence among PWID/LWH (Gwadz et al., 2021). A systematic review and meta-synthesis found stigma related to drug use negatively impacts the ability to adhere to ART among PLWH (Katz et al., 2013). A quantitative study by Shrestha et al. (2019) supports this finding. The authors assessed the relationship between HIV stigma (measured using HIV Stigma Mechanism Measure), drug use (meeting the Diagnostic and Statistical Manual of Mental Disorders [DSM]-V criteria for opioid use disorder), and ART adherence (measured using self-reported percentage of doses taken). Using a sample of HIV-positive patients on methadone therapy (n = 121), the authors found HIV stigma was negatively correlated with ART adherence (AOR = 0.38; $p = 0.02$). Further analysis showed the direct relationship between HIV stigma and ART adherence was significant ($\beta = -0.25$; $p = 0.04$). However, once motivation for ART adherence was added as a mediator this relationship became non-significant ($\beta = -0.13$; $p = 0.06$). Motivation for ART adherence showed a significant mediating effect on the relationship between HIV stigma and ART adherence ($\beta = -0.12$; 95% bootstrap CI = -0.20, -0.06; Sobel $z = -3.78$; $p = 0.04$) (Shrestha et al., 2019).

Stigmas, Mental Health, & HIV Care Engagement

Mental health is also an important factor when looking at the relationship between HIV stigma and HIV care engagement. For instance, Williams et al. (2020) analyzed 2015-2016 MMP data in Florida to examine relationships between HIV stigma and various characteristics, including depression and anxiety. Results showed PLWH with severe depression were significantly more likely to experience overall HIV stigma (AOR = 3.13; 95% CI = 1.38, 7.13), self-image stigma (AOR = 2.81; 95% CI = 1.38, 5.72), and anticipated stigma (AOR = 2.87; 95% CI = 1.38, 5.98) than those without depression. Anxiety was not significantly associated with HIV stigma (Williams et al., 2020).

The association between depression and HIV stigma makes depression an important factor when conducting research related to stigma and ART adherence. For instance, another study in the Southern U.S. investigated the mediating effect of depression on the relationship between HIV stigma and ART adherence. A survey was conducted among PLWH (n = 201) which included the HIV Stigma Scale, the HIV/AIDS Stigma Instrument, the Patient Health Questionnaire (PHQ)-9 (to measure depressive symptoms), care engagement (number of missed appointments in the past six months), and self-reported ART adherence (percentage of doses taken). Results showed HIV stigma was significantly associated with poorer ART adherence (β = 4.90; 95% CI = 0.69, 9.10; $p < 0.05$) and missing an appointment in the past six months (AOR = 0.47; 95% CI = 0.26, 0.85; $p < 0.05$). Depression was significantly negatively associated with ART adherence (β = -6.64; 95% CI = -12.54, -0.65; $p < 0.05$), but was not associated with missed appointments in the past six months (AOR = 0.63; 95% CI = 0.36, 1.71; $p > 0.05$). Mediation analysis found depression was a mediator for the relationship between stigma and ART adherence, but not care engagement (Reif et al., 2019). An analysis of data from the

Women's Interagency HIV Study (WIHS) (n = 862) supports this relationship. Internalized HIV stigma (measured using the HIV Stigma Scale) was significantly associated with low ART adherence (<95% of doses taken) (AOR = 0.61; 95% CI = 0.45, 0.82; $p = 0.001$). Results of mediation analysis showed depression was a mechanism for the relationship between internalized HIV stigma and ART adherence (indirect effect $\beta = -0.05$; 95% CI = -0.11, -0.006) (Turan et al., 2019a).

These studies were conducted among PLWH in general and not specifically in those with substance use disorders or who inject drugs. However, results in PLWH who also use substances have found similar results. For example, interviews conducted with HIV-positive Black and Hispanic women who use substances found heavy substance use reduced adherence to ART. Participants indicated substance use triggered depression, resulting in lack of motivation and self-efficacy to take ART (Gwadz et al., 2016). In another study, Earnshaw et al. (2015) conducted surveys with HIV-positive substance users to measure internalized HIV stigma, internalized substance use stigma, and depression symptoms. Results showed a significant association between these two types of stigma and depression. Further, those who experienced both types of stigma had even higher levels of depression (Earnshaw et al., 2015).

While current research on HIV, drug use, stigma, HIV care engagement, and mental health demonstrates complex interactions, these constructs are often siloed or studied one or two at a time. However, these constructs are not siloed in the real world. Due to limitations in secondary data analysis (i.e., exclusion of drug use- and mental health-related stigma measurements in the existing data), intersecting stigmas will not be addressed in the current study. However, future research should include a combination of these constructs to improve our understanding of how they interact in the context of one another.

Syndemic Theory

The concept of interacting components influencing health outcomes is supported by syndemic theory. In this section, I first provide an overview of syndemic theory and its origins in HIV research. Then, I present models that have expanded on the original syndemic theory model.

Overview of Syndemic Theory

Syndemic theory provides a framework for understanding how multiple diseases and different social conditions interact in synergistic ways to create poorer health outcomes in a population (Singer & Clair, 2003). Conceptualized from medical anthropology, syndemic theory has a long history in HIV research. The term *syndemic* was first applied to HIV/AIDS by Merrill Singer in the early 1990's to explain disparities in AIDS outcomes among urban, poor people of color (Singer, 1994). The term *syndemic* was derived from the Greek words for "working together" (*syn*-) and "the people" (-*demic*) (Singer, 1994, 1996). Singer (1994) suggested that health disparities experienced by urban people of color were a result of poverty, racism, substance use, structural violence, and AIDS "working together," and that to successfully address disparities, these interactions must be considered as a whole. Notably, a syndemic does not simply refer to two co-occurring diseases or conditions (i.e., comorbidities), but to the interaction of these biological diseases with social conditions which result in health consequences (Singer & Clair, 2003). In other words, the interplay between diseases occurs within the context of one's social domain (Wright et al., 2016). These social conditions can include experiences related to one's gender identity, socioeconomic status, geographic location, race/ethnicity, and age.

Application of Syndemic Theory to HIV and Substance Use

Since Singer's initial publication on the topic, the concept of syndemics in HIV/AIDS has been extensively built or expanded upon. Further conceptualizing the syndemic of AIDS and poor inner-city health, Singer (1996) developed the Substance Abuse, Violence, and AIDS (SAVA) Syndemic model. This triangular model, with each piece of the syndemic representing a corner of the triangle, demonstrates how drug use, gang violence, and AIDS interact in ways that precludes each issue from being mutually exclusive (Singer, 1996).

Others have expanded on the SAVA model. For instance, Robinson et al. (2016) developed the Substance Use, Mental Illness, and familial Conflict non-negotiation (SUMIC) Syndemic framework. This framework was developed to explain poor health outcomes among Black PWID/LWH, particularly in women. The authors tested the framework through an analysis of Black participants from the BEACON study (n = 351). Results showed that higher levels of SUMIC syndemic burden, as measured through a latent variable, was significantly associated with lack of viral suppression (>40 copies/mL) and acute care non-utilization when compared to lower levels of SUMIC syndemic burden. In addition, when compared those in the highest SUMIC burden group, women had lower odds than men of being in the lowest burden group (OR = 0.21; 95% CI = 0.01, 0.61; $p < 0.001$) (Robinson et al., 2016). This study demonstrates the syndemic burden of substance use, mental health, and family conflict has adverse effects on HIV-related health outcomes and is also experienced more acutely by women.

González-Guarda et al. (2011) also expanded the SAVA model with the development of the Syndemic Model of Substance Abuse, Intimate Partner Violence, HIV Infection, and Mental Health among Hispanics. This model was developed to address a lack of SAVA models among Hispanic/Latinx populations. The model includes culture as its own social factor to highlight its

important role in the syndemic among Hispanic/Latinx populations. For instance, recent Hispanic/Latinx immigrants to the U.S. may experience challenges to traditional family values (i.e., familism) as the need for dual income reduces the amount of time they can spend with their spouse and children. This challenge can increase stress on family relationships, potentially leading to poor coping behaviors like substance use, depression, or violence. However, cultural factors can also be protective, i.e., family support resulting from familism reduces poor coping behaviors. This model therefore recognizes the importance of culture on how substance use, mental health, violence, and HIV are interpreted and experienced by those affected by the syndemic (González-Guarda et al., 2011).

Another HIV syndemic framework proposed by Perlman & Jordan (2018) explored the syndemic of opioid use, overdose, hepatitis C, and HIV. The authors present each component of the framework and the overlapping structural factors which influence the syndemic as a whole. Structural factors such as insurance coverage, international policies, and economic inequality can contribute to the syndemic by restricting access to treatment of substance use disorder, hepatitis C, and HIV. In addition, unemployment rates, overdose rates, and prescription opioid sales, can be used to predict a population's vulnerability to the syndemic and ultimately may be targeted for public health interventions (Perlman & Jordan, 2018).

As the models presented in this section show, syndemic theory is useful for better understanding the complexity of HIV, drug use, and mental health in the context of various social conditions. Therefore, this study will utilize syndemic theory as a framework for better understanding the syndemic of intravenous drug use, mental health, and HIV stigma.

Limitations in HIV Care Engagement Research Among PWID/LWH

Overall, the current research on mental health and HIV care engagement among PWID/LWH is limited. Most research on PWID/LWH contains sampling bias, since PWID are a difficult population to enroll and retain in research studies (Magnani et al., 2005). Researchers, therefore, frequently use convenience sampling techniques (Kral et al., 2010; Magnani et al., 2005). Even more robust sampling methods, such as respondent-driven sampling, often still contain bias (Collier et al., 2017; Platt et al., 2006; Zeng et al., 2019). Loss to follow-up is also common among PWID (Sordo et al., 2015). Because of these sampling limitations, it is difficult to conclude if barriers to HIV care in the literature (e.g., mental health, stigma, etc.) are applicable to all PWID.

In addition to method limitations, there is a lack of research on the syndemic effects of HIV stigma, IDU, and mental health on HIV care engagement. Most research that includes substance use disorder as a syndemic condition does not differentiate between IDU and other types of substance use (Bhardwaj & Kohrt, 2020; Blashill et al., 2015; Friedman et al., 2015; Glynn et al., 2019; Godley & Adimora, 2020; Illangasekare et al., 2013; McMahon et al., 2019; Quinn et al., 2018; Satyanarayana et al., 2021; Tsuyuki et al., 2017). However, based on studies showing associations between these various syndemic conditions and HIV care engagement, IDU likely presents its own unique challenges and contributions to the HIV and substance use syndemic.

Finally, previous research on PWID/LWH has typically focused on urban centers in the Northeastern U.S. or on the U.S. overall. However, the Southern U.S. is particularly affected by HIV, with higher rates of infection than other regions in the U.S. In addition, PLWH in the

Southern U.S. also have lower rates of care engagement and higher rates of HIV-related stigma than other areas of the U.S. (CDC, 2019a).

Conclusion

There has been a startling increase in incident HIV among PWID in the U.S. over the past decade. This increase makes it more important than ever to better understand the complex syndemic of IDU, mental health, and stigma to ensure those affected receive proper care and have positive health outcomes. Given the high rates of mental health conditions and stigma among PLWH and PWID, there is a lack of research on the associations between IDU, mental health, stigma, and HIV care specifically in PWID/LWH. In addition, we need more generalizable data to further our understanding. The current study aims to address limitations in the literature through using CDC's MMP data, collected from a diverse, population-based sample in three Southern states that includes PWID/LWH, to answer the following research questions:

1. What is the construct validity of a theoretical model of the syndemic burden of mental health, IDU, and HIV stigma?
2. What is the construct validity of a theoretical model of HIV care and coverage?
3. To what extent is the syndemic burden of mental health, IDU, and HIV stigma associated with HIV care and coverage?

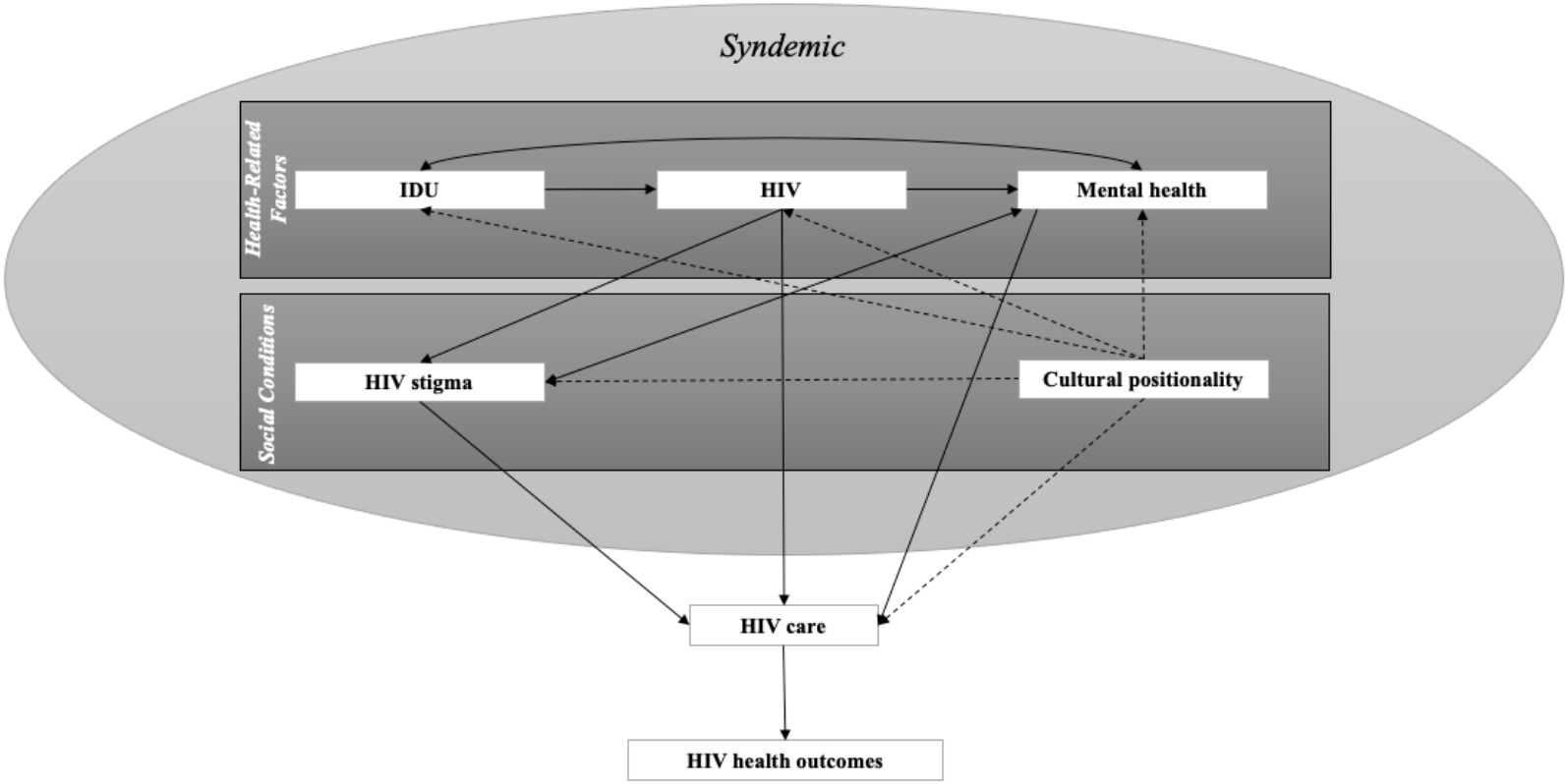
I expect results to show higher levels of syndemic burden are associated with lower levels of HIV care and coverage.

CHAPTER III: ANALYTIC PLAN

Conceptual Model

Syndemic theory is useful for understanding the complexity of co-occurring HIV, drug use, and mental health and adverse social conditions. A conceptual model of the IDU, mental health, and HIV stigma syndemic illustrates this relationship (see Figure 2 below). HIV, IDU, and mental health (in the Health-Related Factors rectangle) and social conditions including HIV stigma and cultural positionality (e.g., gender, race/ethnicity [racism], age, geographic location, educational status, economic status, etc.) (Social Conditions rectangle) are all represented as syndemic by their inclusion in the gray oval. Arrows designate the relationships between each component. The arrow from IDU to HIV indicates the relationship between IDU and HIV infection through needle sharing. Both IDU and HIV have arrows to mental health, as these conditions are associated with negative mental health outcomes such as depression. However, the arrow between IDU and mental health is bi-directional, indicating that either can cause the other (e.g., IDU results in mental health conditions or mental health conditions result in IDU) or the potential cyclical nature of the relationship between these two components (e.g., depression leads to increased drug use, which can lead to greater depression). The arrow from HIV diagnosis to HIV care represents the necessity of HIV care after diagnosis. However, HIV stigma and mental health can influence HIV care. This influence may be cyclical, with HIV stigma and mental health conditions contributing to poor mental health and HIV stigma (indicated through the bidirectional arrow). Cultural positionality, characterized by gender, age, race/ethnicity, education, geographical location, income, etc., influences all aspects of the syndemic (IDU, HIV, mental health, HIV-related stigma) and HIV care outcomes. Finally, HIV care results in HIV-related health outcomes.

Figure 2. Conceptual Model



Note. The gray oval represents the syndemic of HIV, IDU, and mental health (Health-Related Factors) and stigma and cultural positionality (Social Conditions). Solid arrows designate the relationships between each component, with dotted lines representing moderating effects. The syndemic negatively impacts HIV care, resulting in poor HIV-related health outcomes. IDU = intravenous drug use.

Data Source

This secondary data analyses uses data from CDC's Medical Monitoring Project. Since 2004, MMP has complemented the National HIV Surveillance System (NHSS), which collects core characteristics of all PLWH in the U.S. and its territories, by collecting more detailed information on clinical outcomes, HIV care engagement, and health behaviors (CDC, 2015). Between 2004 and 2014, MMP only collected data on PLWH who were engaged in care. In 2015, MMP began a new sampling method, which would include PLWH who are both in and out of care. This study utilizes MMP data collected between 2015 and 2018/9, the most recent years in which data are available.

MMP's expanded sampling method uses two-stage probability sampling of PLWH in and out of care. The first sampling stage, conducted when MMP began in 2004, randomly selected service areas from all 50 states, the District of Columbia, and Puerto Rico. Each service area had a selection probability proportional to the 2002 estimate of the number of persons living with AIDS. This selection process resulted in 20 service areas, with six additional local areas within certain states. However, due to funding cuts, the number of national service areas is currently 23. The second stage of sampling consists of randomly selecting PLWH within each project area sampling frame. Eligible participants (i.e., adults living with HIV who are at least 18-years old and diagnosed prior to the sampling date) are contacted by MMP using contact information from NHSS or other resources (e.g., health care providers, Lexis-Nexis, pharmacy records, etc.). This two-stage sampling method results in a nationally representative sample of ~10,900 HIV-positive adults per year.

Once a participant has provided informed consent, they are scheduled for a structured, computer-assisted interview with a trained interviewer. While the MMP questionnaire is

available in English and Spanish, interpreters can be used for additional languages, if necessary. Each interview lasts 45-55 minutes and participants are given a token of appreciation ($25 cash or equivalent) for their participation. After the interview, medical records from participants' most recent, usual outpatient HIV-care provider are abstracted by trained abstractors. If a participant has never seen a provider, then no abstraction is conducted.

This study utilizes MMP data collected in three Southern states between 2015 and 2018/9. Southern states were selected for this study because the Southern U.S. has the highest number of PLWH compared to other regions of the country with over 460,000 in 2018 (CDC, 2021b). The Southern U.S. also has the highest proportion of new HIV cases, with 51% of all new U.S. cases in 2018 occurring in the South (CDC, 2022b). The three states included in this study are Florida, Georgia, and Virginia.

The total number of PLWH sampled, the resulting overall sample size, and number of those ever-injecting drugs for each of three states included in this study across years are presented in Table 1 below. The overall sample for this study is n = 2,939. Within the overall sample, the number of PLWH who have ever injected drugs is n = 247.

Table 1. MMP Sample 2015-2018/9

MMP Area	Year (*n* participating/*n* sampled)						Total PWEID (*n*)
	2015	2016	2017	2018	2019	Total	
Florida	299/800	333/800	292/800	339/800	315/800	1,578/4,000	133
Georgia	164/500	207/500	211/500	176/500	--	758/2,000	59
Virginia	111/400	158/400	166/400	168/400	--	603/1,600	55
Overall	*574/1,700*	*698/1,700*	*669/1,700*	*683/1,700*	*315/800*	*2,939/7,600*	*247*

Note. MMP = Medical Monitoring Project. PWEID = people who ever injected drugs. (CDC, 2021a).

This study was submitted to the University of North Carolina Greensboro's (UNCG) Institutional Review Board (IRB). The IRB determined this study was not human research, since the study uses deidentified secondary data (Study #:21-0158) (see APPENDIX B: UNG IRB DETERMINATION).

Measures

A summary of variables used in this study and how they were measured is presented in Table 2 below.

Table 2. Study Variables

Variable Name	Measure
Age	Years
Race	Non-Hispanic Black, Non-Hispanic White, Non-Hispanic Other, Hispanic/Latinx
Education	Highest level of education completed (Less than high school; High school or GED; Some College; Bachelor's degree or higher)
State	State (Florida; Georgia; Virginia)
Gender	Male, Female, Transgender
Insurance type	Employer-sponsored insurance (i.e., private insurance or TRICARE), no employer-sponsored insurance
HIV care retention	Missed any appointments in the past 12-months (Yes/No)
ART adherence	% days with no missed doses over the past 30 days ([30 - number of days with missed doses] / 30 * 100)
Viral suppression at most recent test	<200 copies/mL blood (Yes/No)
Depression symptoms	PHQ-8 score (0-24)
Anxiety symptoms	GAD-7 score (0-21)
Current intravenous drug use	Injected drugs in the past 12-months (Yes/No)
Ever intravenous drug use	Ever injected drugs (Yes/No)
HIV stigma	Modified HIV Stigma Scale score (0-100)

Note. GED = General Education Diploma. ART = antiretroviral therapy. MMP = Medical Monitoring Project. PHQ = Personal Health Questionnaire. GAD = General Anxiety Disorder.

Intravenous drug use. Ever IDU was assessed by asking participants if they had ever injected drugs or had someone else inject them with drugs that were not for medical purposes. Participants could respond *yes, no, don't know,* or refuse to answer. Current IDU was assessed by asking participants if they had injected any drug in the past 12 months that was not for medical purposes. Response options were the same as for ever (lifetime) IDU.

Anxiety. Anxiety symptoms were measured using the General Anxiety Disorder (GAD)-7 scale (Spitzer et al., 2006). This scale asks participants how often they were bothered by seven symptoms of anxiety over the last two weeks. Each item is scored on a four-point Likert scale (0 Not at all, 1 Several days, 2 More than half the days, 3 Nearly every day). Items are then summed resulting in a score between 0 and 21, with higher scores indicating higher levels of anxiety symptoms. I will interpret a score of 10 or higher as generalized anxiety disorder. A previous study has reported an 89% sensitivity and 82% specificity for diagnosing generalized anxiety disorder using a GAD-7 score of 10 or higher (Spitzer et al., 2006). Reported internal consistency for the GAD-7 is high (Cronbach's $\alpha = 0.92$) (Spitzer et al., 2006).

Depression. Depression symptoms were measured using the PHQ-8 (Kroenke et al., 2009). Similar to the GAD-7, the PHQ-8 asks participants how frequently they felt symptoms of depression over the past two weeks. The scale is scored on a four-point Likert scale (0 Not at all, 1 Several days, 2 More than half the days, 3 Nearly every day). Items are summed to create a score between 0 and 24, with higher scores indicating higher levels of depression symptoms. As in previous studies, I will interpret a score of 10 or greater as major depression (Shin et al., 2019). Internal consistency for the PHQ-8 is high (Cronbach's $\alpha = 0.86$) (Shin et al., 2019).

HIV-related stigma. HIV-related stigma was measured using a modified version of the HIV Stigma Scale (Wright et al., 2007). The modified scale consists of 10 items across four subscales: personalized stigma, disclosure concerns, negative self-image, and concern about negative public attitudes. Each item is scored on a five-point Likert scale (1 Strongly disagree, 2 Somewhat agree, 3 Neutral, 4 Somewhat agree, 5 Strongly agree). Subscales are scored on a continuous scale from 0 to 20 or 30, based on the number of questions for each subscale. For instance, the personalized stigma subscale has three questions and is therefore scored 0 to 30. The overall scale has final scores ranging from 0 to 100, with higher scores indicating higher levels of stigma. Internal consistency of the HIV stigma scale is high (Cronbach's $\alpha = 0.72\text{-}0.84$) (Wright et al., 2007).

HIV Care and coverage. HIV care and coverage outcomes include care retention, ART adherence, viral suppression, and insurance type. Care retention was self-reported as not having any missed HIV-related appointments in the past 12 months.

ART adherence was defined as the self-reported percentage of days with no missed doses over the past 30-days ([30 - number of days with missed doses] / 30 * 100). Viral suppression was defined as a viral load <200 copies/mL blood at the most recent viral load test in the medical record.

Insurance type was divided into two categories: employer-sponsored insurance or no employer-sponsored insurance. Participants reporting any private insurance or TRICARE coverage were considered to have employer-sponsored insurance. Those not reporting either of these types of insurance were placed into the no employer-sponsored insurance category.

Demographics. Demographic characteristics include age, race/ethnicity, education level, state, and gender. Age is reported in years. Race/ethnicity is categorized into non-Hispanic

Black/African American, non-Hispanic White, non-Hispanic Other, and Hispanic/Latinx. Education is divided into four categories: less than high school (never attended school; grades 1-8; grades 9-11), high school (grade 12; General Education Diploma [GED]), some college (some college; associate's degree; technical degree), and Bachelor's degree or higher (Bachelor's degree; any post-graduate studies). State is the state from which the data were received (i.e., Florida, Georgia, or Virginia). Gender is reported as male, female, or transgender.

Data Analyses

All analyses were weighted to account for the two-stage sampling design of MMP, multiplicity, and non-response bias (Johnson et al., 2020). Analyses were conducted using SAS v. 9.4 (Cary, NC) and Mplus v. 8.7 (Muthén & Muthén, 2017). Results with a p-value < 0.05 were interpreted as statistically significant.

Univariate and Bivariate analysis

Descriptive statistics for the sample were calculated for both unweighted (frequencies, percentages, and means) and weighted (percentages and means only) data overall and by intravenous drug use status. A table describing the sample characteristics is presented below (see Table 3).

Weighted correlations between study variables were analyzed using Pearson's r, point-biserial correlations (r_{pb}), and tetrachoric correlations (r_{tet}). These correlations provide the direction and degree of the relationships between variables.

Table 3. Sample Characteristics ($n_{unweighted}$ = 2,939)

Characteristic	Unweighted Overall *n* (%) or *Mean ± SE*	Weighted Overall % or *Mean ± SE*	Weighted Never Injected Drugs % or *Mean ± SE*	Weighted Ever Injected Drugs % or *Mean ± SE*	Weighted Currently Injecting Drugs % or *Mean ± SE*
Age (years)	48.6 ± 0.2	48.4 ± 0.3	48.2 ± 0.3	50.8 ± 0.8	41.1 ± 1.6
missing	28				
State					
Florida	1,578 (53.7)	60.0	60.0	59.8	56.9
Georgia	758 (25.8)	27.9	28.0	26.9	24.9
Virginia	603 (20.5)	12.1	12.0	13.3	18.2
missing	0				
Race/Ethnicity					
Non-Hispanic White	680 (23.1)	25.1	23.3	43.9	43.8
Non-Hispanic Black	1,659 (56.5)	54.4	56.5	31.6	27.5
Non-Hispanic Other	173 (5.9)	5.2	4.9	8.8	11.6
Hispanic/Latinx	427 (14.5)	15.4	15.3	15.7	17.1
missing	0				
Education					
Less than high school	558 (19.1)	17.9	18.1	15.2	11.7
High school	750 (25.7)	26.0	26.3	23.2	17.6
Some college	1,004 (34.4)	35.0	34.3	42.4	44.5
Bachelor's degree	608 (20.8)	21.1	21.3	19.2	26.2
missing	19				
Gender					
Male	1,996 (67.9)	72.4	71.4	82.7	90.6
Female	913 (31.1)	26.6	27.5	16.8	6.9
Transgender	30 (1.0)	1.0	1.1	0.5	2.5
missing	0				
Employer-sponsored insurance					
Yes	1,127 (38.7)	38.5	39.0	32.7	37.1
No	1,789 (61.4)	61.5	61.0	67.3	62.9
missing	23				

Table 3. Sample Characteristics ($n_{unweighted}$ = 2,939), cont.

Characteristic	Unweighted Overall *n* (%) or *Mean ± SE*	Weighted Overall % or *Mean ± SE*	Weighted Never Injected Drugs % or *Mean ± SE*	Weighted Ever Injected Drugs % or *Mean ± SE*	Weighted Currently Injecting Drugs % or *Mean ± SE*
Missed any appointments in past 12 months					
Yes	644 (22.2)	22.9	22.6	25.4	57.3
No	2,251 (77.8)	77.1	77.4	74.6	42.7
missing	44				
% days adherent to ART over past 30 days (%)	95.6 ± 0.2	95.4 ± 0.3	95.5 ± 0.3	94.2 ± 1.0	86.0 ± 3.5
missing	182				
Viral suppression (<200 copies/mL) at most recent lab test					
Yes	2,352 (88.5)	86.8	87.0	84.9	77.3
No	306 (11.5)	13.2	13.0	15.1	22.7
missing	281				
Anxiety (GAD-7) score	3.3 ± 0.1	3.3 ± 0.1	3.1 ± 0.1	4.7 ± 0.4	5.7 ± 0.9
missing	38				
Depression (PHQ-8) score	3.1 ± 0.1	3.0 ± 0.1	2.9 ± 0.1	4.3 ± 0.5	5.4 ± 1.0
missing	45				
HIV stigma score	41.9 ± 0.4	41.1 ± 0.5	41.1 ± 0.5	40.8 ± 1.8	38.9 ± 2.6
missing	131				
IDU in past 12 months					
Yes	53 (1.8)	1.8	--	20.7	--
No	2,849 (98.2)	98.2		79.3	
missing	37				
Ever IDU					
Yes	247 (8.5)	8.7	--	--	--
No	2,655 (91.5)	91.3			
missing	37				

Note. ART = antiretroviral therapy. GAD = General Anxiety Disorder. HIV = human immunodeficiency virus. IDU = intravenous drug use. PHQ = Personal Health Questionnaire. SE = standard error.

Structural Equation Model Analysis

Structural equation modeling (SEM) uses a combination of regression and factor analysis to assess relationships between variables. In addition, it allows for analysis of a latent variable, which is important to the purpose of this study because syndemic burden is not directly observable. It can, however, be manifested using observable variables such as IDU, levels of depression and anxiety symptoms, and relevant demographic characteristics. SEM is also useful for this analysis because it allows for covariance between variables without having to specify the relationship between them (e.g., the relationship between IDU and mental health is correlated, but direction of the relationship is not easily specified).

Using SEM to assess the syndemic effects of HIV, general substance use, and mental health has been established in the literature. For instance, McMahon et al. (2019) examined the cross-sectional associations between the syndemic factors of HIV, substance use dependence, mental health, HIV stigma, social support, and demographic characteristics with ART adherence and viral load among heterosexual men using a SEM. Using SEM allowed the authors to test direct and indirect effects between syndemic and HIV care outcomes. Tsuyuki et al. (2017) also used SEM, in the form of confirmatory factor analysis (CFA), to assess differences in the syndemic effects of substance use disorder, violence, and mental health among heterosexual men, heterosexual women, and MSM living with HIV. The authors utilized CFA to test if measures of substance use disorder, experiencing violence, and mental health were adequate to measure the syndemic in each population (Tsuyuki et al., 2017).

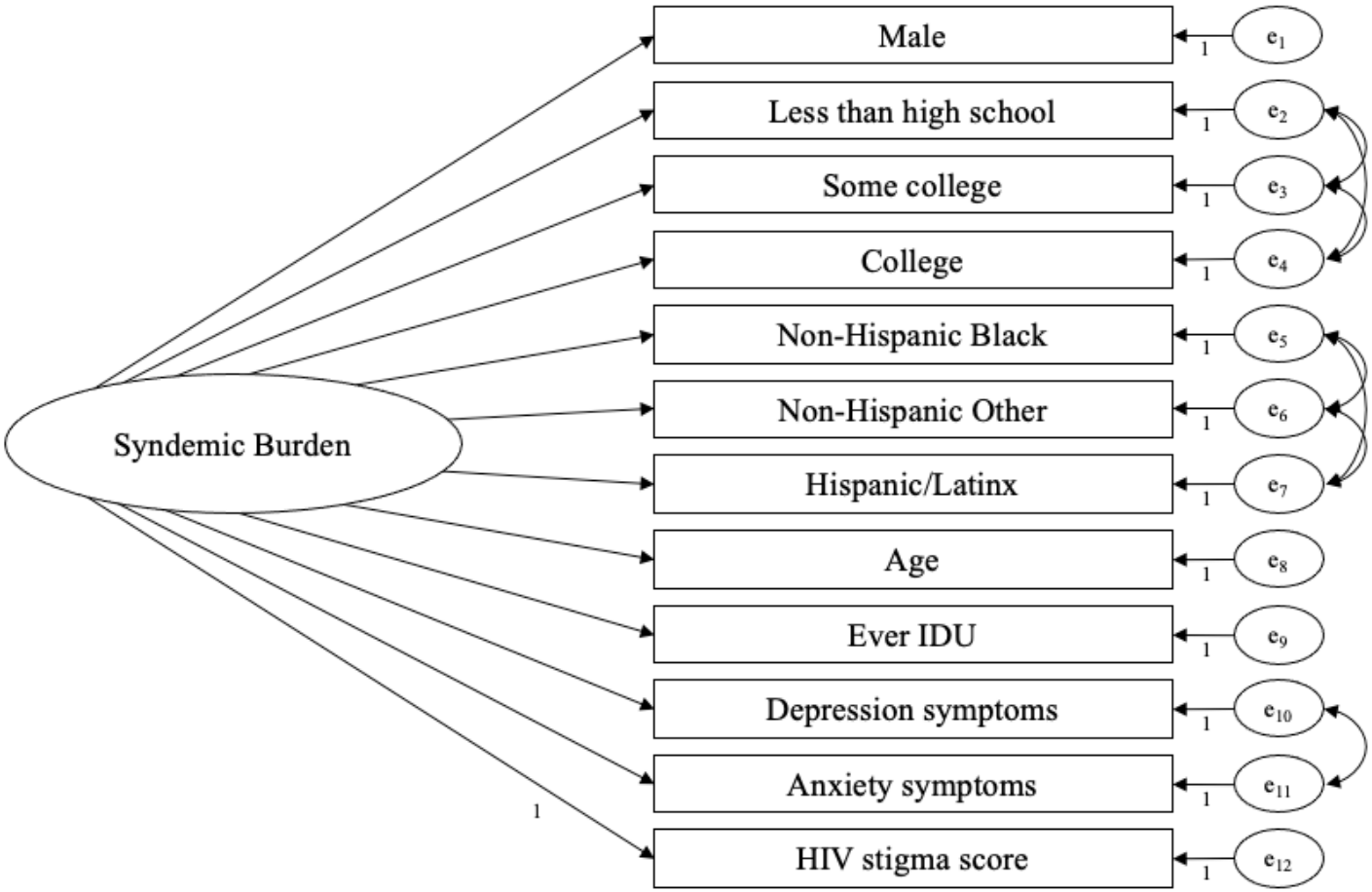
For this analysis, I examine the construct validity of syndemic burden and HIV care using CFA. Then, I assess the relationship between these two constructs using a SEM.

Confirmatory Factor Analyses (CFA)

Similar to Tsuyuki et al. (2017), I first assess the measurement models of syndemic burden and HIV care using CFA. CFA provides a statistical method to test the fit of a hypothesized model to the data and to assess construct validity of a latent variable (Huck, 2012). In my proposed CFA model for syndemic burden, I include indicators which are hypothesized to be components of syndemic burden (see Figure 3 below). Demographic characteristics (i.e., gender, race/ethnicity, education level, and age) and HIV stigma are included as measures of social conditions. IDU, depression symptoms, and anxiety symptoms are included as health-related factors.

Residuals for indicators stemming from the same categorical variable (e.g., non-Hispanic Black and Hispanic/Latinx indicators from the race/ethnicity variable) were allowed to correlate to adjust for the resulting residual correlation between these indicators. In addition, the residuals for anxiety and depression symptom scores were correlated since anxiety and depression are often comorbid and share similar symptoms, neurobiological processes, and measurement scales (Kalin, 2020).

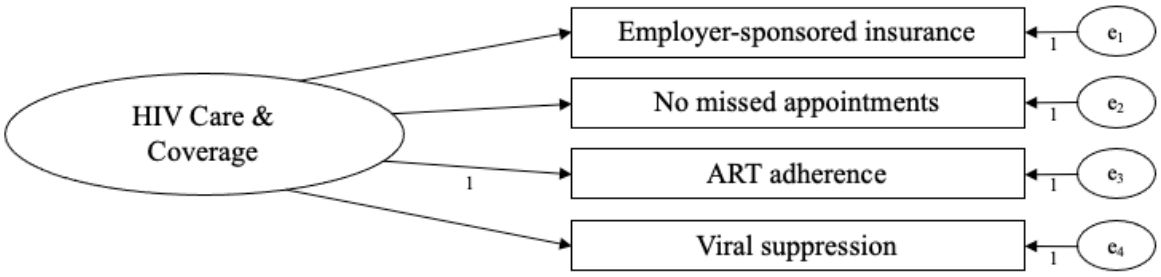
Figure 3. Confirmatory Factor Analysis for Syndemic Burden



Note. Syndemic burden is manifested through indicators for gender (ref. female/transgender), education (ref. high school), race/ethnicity (ref. non-Hispanic White), age, IDU status (ref. never injected drugs), depression symptoms, anxiety symptoms, and HIV stigma score. Syndemic burden is scaled to HIV stigma score (factor loading for HIV stigma scale = 1). Double-headed arrows indicate correlation between residuals. e = error. IDU = intravenous drug use. Ref. = referent category.

The concept of HIV care is often measured using individual measures of the HIV care continuum. For instance, many studies discussed in Chapter 2 utilize ART adherence or viral load as proxy measures for the concept of HIV care. However, using a latent variable for the concept of HIV care, which includes stages of the HIV care continuum and insurance coverage, more accurately portrays the true complexity of this concept. Since SEM and CFA calculate all coefficients at once, instead of one at a time as in multiple regression, it accounts for the variances of all included indicators to address any potential interdependence of HIV care engagement indicators (i.e., no missed appointments, ART adherence, and viral suppression) (Beran & Violato, 2010). In addition, latent variables help eliminate measurement errors associated with assessing each measure individually (Lei & Wu, 2007). In my proposed model for HIV care and coverage, I include insurance coverage, care retention, ART adherence, and viral suppression (see Figure 4 below).

Figure 4. Confirmatory Factor Analysis for HIV Care and Coverage



Note. HIV care and coverage is manifested through indicators for employer-sponsored insurance (ref. no employer-sponsored insurance), no missed appointments in the past 12 months (ref. missed appointment in the past 12 months), ART adherence, and viral suppression (ref. no viral suppression). HIV care and coverage is scaled to ART adherence (factor loading for ART adherence = 1). ART adherence was defined as percentage of days with no missed doses over the past 30 days. Viral suppression was defined as <200 copies HIV/mL blood at most recent lab test. ART = antiretroviral therapy. e = error. Ref. = referent category.

Goodness of fit for each CFA was assessed using model χ^2, Steiger-Lind root mean square error of approximation (RMSEA), Bentler comparative fit index (CFI), and standard root mean square residual (SRMR). An insignificant χ^2 ($p > 0.05$) or values of ≤0.06 for RMSEA, ≤0.08 for SRMR, and ≥0.90 for CFI were interpreted as good model data fit (Lei & Wu, 2007). If either model was not a good fit for the data, they were modified based on theory (e.g., allowing additional residual correlations among related indicators) or empirical evidence (e.g., removing variables with non-significant path coefficients) (Kline, 2015).

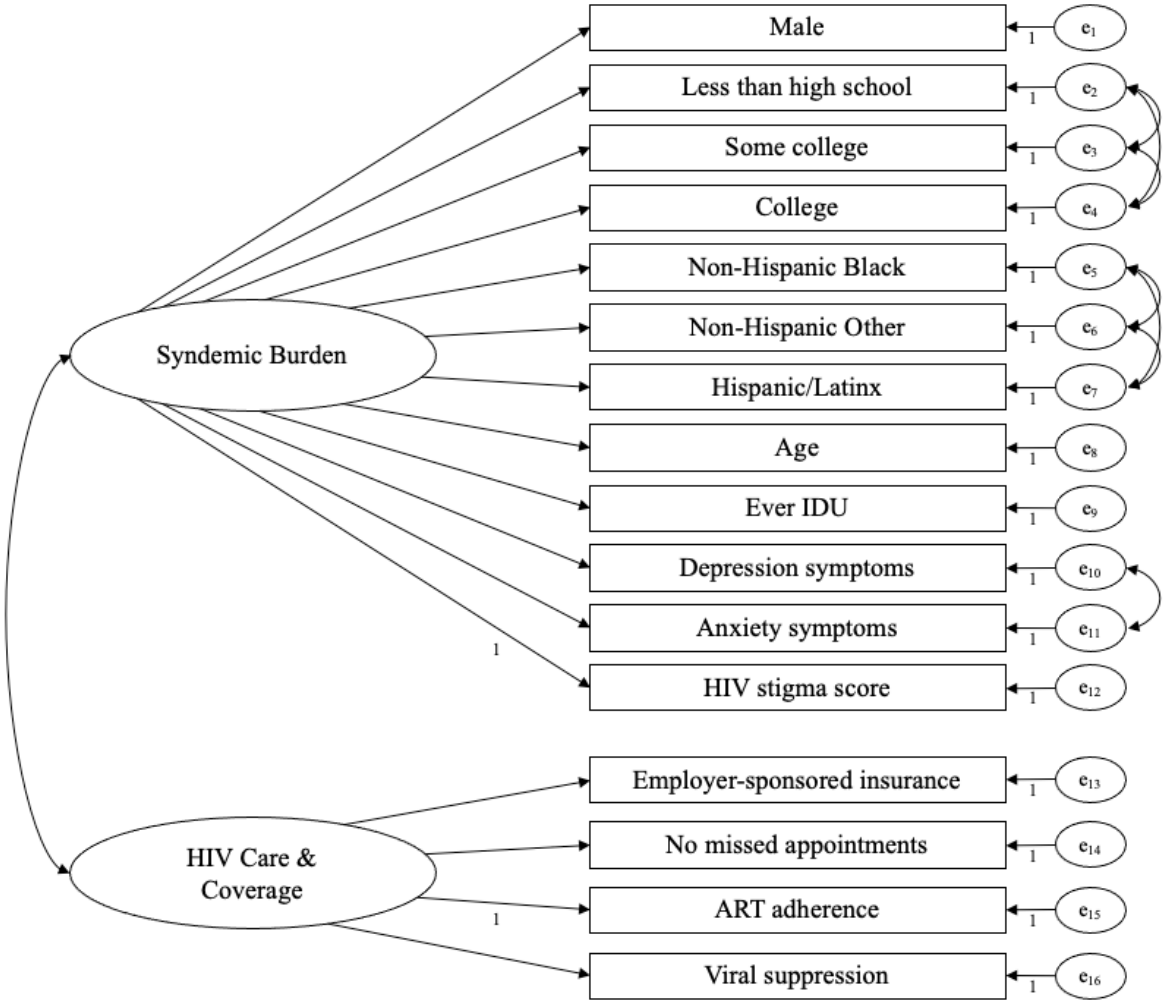
Structural Model

The structural model assesses the association between syndemic burden and HIV care and coverage. The latent variables (syndemic burden and HIV care and coverage) are manifested in the model through the observational variables tested in the CFAs above. Syndemic burden was hypothesized to be negatively associated with HIV care and coverage (see Figure 5). The proposed model has 136 observations and 40 parameters to be estimated. Therefore, the model is overidentified ($df_M = 96$) meaning parameters can be estimated (Lei & Wu, 2007).

The resulting tables included unstandardized and standardized coefficients for each of the arrows between measured constructs and latent variables. The coefficients show the direction and magnitude of the relationship demonstrated by the arrow and whether that relationship is statistically significant. Unstandardized coefficients are interpreted as typical regression coefficients, with the referent indicator as the scale for the latent variable. Standardized coefficients, on the other hand, allow comparisons of the magnitude of influence between indicators to be made. In addition to calculating coefficients for each arrow between indicators and latent variables, a coefficient representing the covariance (unstandardized) or correlation (standardized) was calculated for the arrow linking the latent variables (i.e., syndemic burden

and HIV care) together. Goodness of fit was assessed using the same methods as for the CFAs above.

Figure 5. Structural Equation Model



Note. Syndemic burden is manifested in the model through IDU, depression symptoms, anxiety symptoms, HIV stigma, and demographic characteristics. This syndemic burden is associated with HIV care and coverage, manifested through care retention, ART adherence, viral suppression, and insurance coverage. ART = antiretroviral therapy. e = error. IDU = intravenous drug use.

There is some debate on what constitutes a sufficient sample size for SEM. Some researchers argue the minimum sample size should be n = 200. Others argue it should be at least 5x larger than the number of parameters (for this analysis 5 x 40 = 200) (Lei & Wu, 2007). Given my sample size of n = 2,939, I meet both these parameters.

Results are presented in tables, figures, and summary text.

Threats to Validity

The validity of this study may be threatened by biases inherent to cross-sectional survey research and SEM methods. Since MMP surveys were conducted cross-sectionally, results of this analysis cannot be used to infer causality, i.e., temporal relationships between factors cannot be determined. Also, this analysis combined data from surveys which were conducted across three years; therefore, any events which occurred over the course of the three years may affect participant responses (e.g., if a new HIV treatment became available).

Though validated measures were utilized by MMP (e.g., PHQ-8), no measure can perfectly assess psychosocial constructs. In addition, some measures were self-reported (e.g., number of days with missed doses of ART), which may be affected by response bias (e.g., recall or social-desirability biases).

The SEM used in this study is based on theory and supported by previous research; however, there is a risk for confirmation bias since there could be valid, alternative models that were not tested. Omission of constructs in MMP data relevant to the analysis and/or omission of any factor that could be an alternative explanation for an association may result in specification errors and/or confounding. Though efforts will be made to adjust for missing data and outliers, as for any statistical analysis, these may affect results.

Finally, though results are generalizable to PLWH in the Southern U.S., they may not be applicable to PLWH everywhere in the U.S. or in other countries.

CHAPTER IV: CONSTRUCT VALIDITY OF A THEORETICAL MODEL FOR THE SYNDEMIC BURDEN OF INTRAVENOUS DRUG USE, MENTAL HEALTH, AND HIV STIGMA

Abstract

The syndemic of IDU, mental health, and HIV stigma contributes to poorer health outcomes among PWID/LWH. Therefore, it is important to try and understand these interconnected factors and the context in which they exist. This study tests the construct validity of a theoretical model of the syndemic burden of IDU, mental health, and HIV stigma using confirmatory factor analysis. Indicators included health-related variables (i.e., depression symptoms, anxiety symptoms, and ever IDU) and social conditions (i.e., gender, education, age, race/ethnicity, and HIV stigma). Results showed female gender, Black race/ethnicity, and less than high school education were associated with greater syndemic burden. However, the largest indicators for syndemic burden were HIV stigma, depression symptoms, and anxiety symptoms, with higher levels of these factors associated with higher levels of syndemic burden. These factors may therefore be targets for intervention.

Key Words: HIV, syndemic, mental health, stigma, substance use

Introduction

Since 2014, the proportion of new HIV diagnoses attributable to intravenous drug use (IDU) has increased 9% (CDC, 2020c), and is increasingly concentrated among whites (44.9% of new HIV infections among PWID) and cisgender men (57.5%) (CDC, 2020a). The recent increase in people who inject drugs and are living with HIV (PWID/LWH) has reignited the urgency among researchers and public health practitioners to understand and address these

conditions. However, the relationship between HIV and IDU is complicated. Multiple factors contribute not only to increased incidence of HIV among PWID, but also poorer health outcomes among PWID who are LWH. For instance, research has shown higher rates of depression and anxiety among PWID/LWH compared to those who do not inject drugs and are not living with HIV (Jones et al., 2010; Wisniewski et al., 2005). These mental health conditions among PWID/LWH are associated with increased risk of needle sharing, poor ART adherence, and low rates of viral suppression among PWID (Bazzi et al., 2019; Conner et al., 2008; Himelhoch et al., 2007; Mizuno et al., 2015; Robinson & Knowlton, 2016; Waldrop-Valverde & Valverde, 2005).

Stigma further complicates associations of mental health, HIV, and IDU. Stigma is any belief which results in either the perception of or actual loss of status or social standing at the individual or structural level (Phelan et al., 2014). An individual may experience stigma as a result of interactions with others or negative self-perception. For instance, poor treatment by HIV medical providers due to stigmas associated with HIV diagnosis, drug use, or both, can cause PWID/LWH to not disclose their drug use or not see a provider at all, ultimately resulting in poorer HIV-related outcomes (Gwadz et al., 2016; Koester et al., 2019). In addition, poor treatment by providers or not seeing a provider can cause PWID/LWH to feel like "bad patients," which contributes to internalized stigma and shame (the emotional response to stigma) (Hutchinson & Dhairyawan, 2017). Therefore, in addition to poorer HIV-related outcomes, stigma and its associated shame can also worsen mental health conditions, such as depression and anxiety (Earnshaw et al., 2015; McMahon et al., 2019; Reif et al., 2019; Turan et al., 2019a; Williams et al., 2020).

Because the interplay of mental health and stigma may contribute to poorer health outcomes among PWID/LWH, it is important to try and improve our understanding of this

interplay and the context in which it exists. Syndemic theory provides a framework for understanding how multiple diseases and different social conditions interact in synergistic ways to create poorer health outcomes in a population (Singer & Clair, 2003). Conceptualized from medical anthropology, syndemic theory has a long history in HIV research. Singer (1994), who first applied syndemic theory to HIV, suggested health disparities experienced by urban people of color were a result of poverty, racism, substance use, structural violence, and AIDS "working together," and that to successfully address disparities, these interactions must be considered as a whole (Singer, 1994).

Since Singer's initial publication on the topic, the concept of syndemics in HIV research has been extensively expanded upon. Further conceptualizing the syndemic of AIDS and poor urban health, Singer (1996) developed the Substance Abuse, Violence, and AIDS (SAVA) Syndemic model to demonstrate how drug use, gang violence, and AIDS interact in ways that precludes each issue from being mutually exclusive. Others have expanded on this model. For instance, Robinson and colleagues (2016) developed the Substance Use, Mental Illness, and familial Conflict non-negotiation (SUMIC) syndemic framework to explain poor health outcomes among Black PWID/LWH. González-Guarda, Florom-Smith, and Thomas (2011) also expanded the SAVA model with the development of the Syndemic Model of Substance Abuse, Intimate Partner Violence, HIV Infection, and Mental Health among Hispanics, which includes culture as its own social factor to highlight its important role in the syndemic among Hispanic/Latinx populations. Finally, a framework proposed by Perlman and Jordan (2018) explored the syndemic of opioid use, overdose, hepatitis C, and HIV by including structural factors such as insurance coverage, international policies, and economic inequality as contributors to the syndemic.

These models demonstrate the utility of syndemic theory for better understanding the complexity of health-related conditions (i.e., HIV, drug use, and mental health) in the context of cultural positioning and social conditions. Notably, however, stigma is not regularly included in these models, despite its importance as a social determinant of health, due to its influence on cultural norms and institutional policies (Hatzenbuehler, 2018; Hatzenbuehler et al., 2013), and its association with mental health conditions and HIV care among PWID/LWH. In addition, most research that includes substance use disorder as a syndemic condition does not differentiate between IDU and other types of substance use, despite IDU likely presenting its own unique challenges and contributions to the HIV and substance use syndemic. Finally, studies focusing on PWID/LWH often only include those already engaged in care or participating in research. To address these limitations, the current study models the syndemic burden of IDU, mental health, and HIV stigma among a diverse, representative sample of PLWH, which includes PWID/LWH. The overall purpose of this study is to develop and test the construct validity of a theoretical model of the syndemic burden of IDU, mental health, and HIV-related stigma.

Methods

Data Source and Measures

Analysis was conducted using data from the Centers for Disease Control and Prevention's (CDC) Medical Monitoring Project (MMP). Since 2004, MMP has complemented the National HIV Surveillance System (NHSS), which collects core characteristics of all PLWH in the U.S. and its territories, by collecting more detailed information on clinical outcomes, HIV care engagement, and health behaviors (CDC, 2015). Between 2004 and 2014, MMP only collected data on PLWH who were engaged in care. In 2015, MMP began a new sampling method, which would include PLWH who are both in and out of care, allowing for a nationally

representative sample of PLWH in the U.S. Since the current study was part of a larger project to understand associations of substance use and mental health with the HIV care continuum in three states in the U.S. South, this study utilizes MMP data collected from three Southern MMP project areas (Florida, Georgia, and Virginia) between 2015 and 2018/9, the most recent years in which data are available. These states were selected for analysis since the Southern U.S. has the highest number of new diagnoses of HIV and some of the lowest rates of care engagement for PLWH (CDC, 2022b).

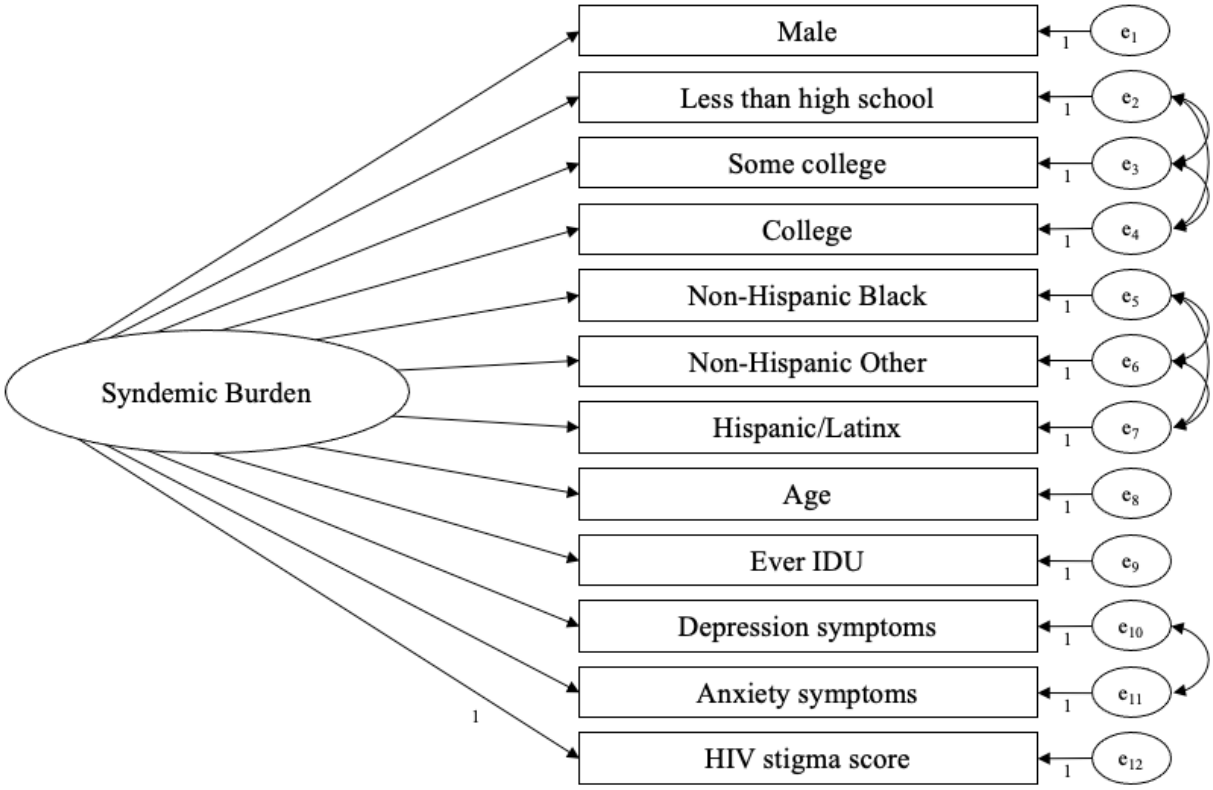
Measures for this analysis were selected based on the health-related factors and social conditions theoretically involved with the syndemic of IDU, mental health, and HIV stigma. Intravenous drug use was assessed by asking whether participants had ever injected drugs or been injected with drugs by someone else not for medical purposes. Mental health measures included the Personal Health Questionaire-8 (PHQ-8) for depression symptoms and the General Anxiety Disorder-7 (GAD-7) for anxiety symptoms. Both the PHQ-8 and GAD-7 ask participants about depression and anxiety symptoms, respectively, that they have experienced over the past two weeks. The PHQ-8 is measured on a scale of zero to 24, with higher scores indicating higher levels of depression symptoms (Kroenke et al., 2009). The GAD-7 scale is scored similarly but ranging from zero to 21 (Spitzer et al., 2006). HIV stigma was measured using a modified version of the HIV Stigma Scale (Wright et al., 2007). This scale asks for level of agreement (strongly disagree, disagree, agree, or strongly agree) with 10 statements covering personalized stigma, HIV diagnosis disclosure, negative self-image, and public attitudes towards HIV. Scores for the HIV Stigma Scale range from 0-100, with higher scores indicating higher levels of stigma.

Demographic characteristics included age, race/ethnicity, level of education, state, and age. Age is reported in years. Race/ethnicity was categorized into non-Hispanic Black/African American, non-Hispanic White, non-Hispanic Other, and Hispanic/Latinx. Education was divided into four categories: less than high school, high school or GED, some college, and Bachelor's degree or higher. State was the state from which the data were received (i.e., Florida, Georgia, or Virginia). Gender was reported as male, female, or transgender. Due to a small sample size of transgender persons (n = 30), female and transgender persons were combined into one referent category.

Model Structure

The proposed model for syndemic burden included health-related and social indicators consistent with syndemic theory (see Figure 6 below). Social indicators included HIV stigma, gender (referent indicator: female/transgender), level of education (referent indicator: high school education), race/ethnicity (referent indicator: non-Hispanic White), and age. These indicators were included in the model as measures of cultural positionality or social location. Health-related indicators included ever injecting drugs, depression symptoms, and anxiety symptoms. Residuals for indicators stemming from the same categorical variable (e.g., non-Hispanic Black and Hispanic/Latinx indicators from the race/ethnicity variable) were allowed to correlate to adjust for the resulting residual correlation between these indicators. In addition, the residuals for anxiety and depression symptom scores were correlated since anxiety and depression are often comorbid and share similar symptoms, neurobiological processes, and measurement scales (Kalin, 2020). Weighted correlation between these variables further supported this relationship ($r = 0.71$; $p < 0.001$). To identify the model to allow for parameter estimates, the latent variable for syndemic burden was scaled to HIV stigma score.

Figure 6. Proposed CFA Model for Syndemic Burden



Note. Syndemic burden is manifested through indicators for gender (ref. female/transgender), education (ref. high school), race/ethnicity (ref. non-Hispanic White), age, IDU status (ref. never injected drugs), depression symptom score, anxiety symptom score and HIV stigma score. Double-headed arrows indicate correlation between residuals. Syndemic burden is scaled to HIV stigma score (factor loading for HIV stigma = 1). e = error. IDU = intravenous drug use. Ref. = referent category.

Analysis

All analyses were weighted to account for MMP's two-stage probability sample design, the potential for participants to be included more than once across survey years, and non-response bias (Johnson et al., 2020). Sample characteristics were assessed using unweighted frequencies and weighted percentages, means, and standard errors. Weighted correlations between study variables were analyzed using Pearson's *r* for continuous variables, or point-biserial (r_{pb}), polychoric (r_{pc}), polyserial (r_{ps}), and tetrachoric correlations (r_{tet}) as appropriate for dichotomous, categorical, or ordinal variables.

For the confirmatory factor analysis (CFA), unstandardized and standardized coefficients were calculated using maximum likelihood estimation with robust standard errors (MLR) for each parameter of the model. Model fit was assessed using RMSEA, CFI, χ^2, and SRMR. Thresholds for good model fit were selected based on previously reported thresholds and were defined as RMSEA ≤0.06, CFI ≥0.90, an insignificant χ^2, and SRMR ≤0.08 (Lei & Wu, 2007). It should be noted that although results of the χ^2 for model fit are reported, they were not used to accept or reject model fit as χ^2 is highly affected by large sample sizes and indicators that are highly correlated.

A *p*-value of $p < 0.05$ was considered statistically significant. Analyses were conducted using SAS v.9.4 (Cary, NC) and Mplus v.8.7 (Muthén & Muthén, 2017).

Results

Overall, participants ($n_{unweighted}$ = 2,939) were mostly male (72.4%), had a mean age of 48.6 years, and were non-Hispanic Black (54.4%) (see Table 4 below). Over half of participants had at least some college education (56.1%). Overall mean depression (3.0) and anxiety (3.3) symptom scores were low, as was the overall mean HIV stigma score (41.1). Ever injecting drugs was reported by 8.7% of participants.

Table 4. Sample Characteristics ($n_{unweighted}$ = 2,939)

Characteristic	Unweighted *n* (weighted %) or weighted mean ± SE
Age (years)	48.6 ± 0.2
missing	28
State	
Florida	1,578 (60.0)
Georgia	758 (27.9)
Virginia	603 (12.1)
missing	0
Race/Ethnicity	
Non-Hispanic White	680 (25.1)
Non-Hispanic Black	1,659 (54.4)
Non-Hispanic Other	173 (5.2)
Hispanic/Latinx	427 (15.4)
missing	0
Education	
Less than high school	558 (17.9)
High school	750 (26.0)
Some college	1,004 (35.0)
Bachelor's degree	608 (21.1)
missing	19
Gender	
Male	1,996 (72.4)
Female	913 (26.6)
Transgender	30 (1.0)
missing	0
Anxiety (GAD-7) score	3.3 ± 0.1
missing	38
Depression (PHQ-8) score	3.0 ± 0.1
missing	45
HIV stigma score	41.1 ± 0.5
missing	131
Ever IDU	
Yes	247 (8.7)
No	2,655 (91.3)
missing	37

Note. GAD = General Anxiety Disorder. HIV = human immunodeficiency virus. IDU = intravenous drug use. PHQ = Personal Health Questionnaire. SE = standard error.

Weighted correlations (see Table 5) between study variables showed a significant correlation between depression and anxiety symptoms ($r = 0.71$; $p < 0.001$). Depression and anxiety symptoms were also significantly correlated with HIV stigma ($r = 0.31$ and $r = 0.30$, respectively; both $p < 0.001$) and ever IDU ($r_{pb} = 0.11$ and $r_{pb} = 0.13$; both $p < 0.01$). Ever IDU was also significantly positively correlated with non-Hispanic White ($r_{tet} = 0.29$; $p < 0.001$) and male ($r_{tet} = 0.18$; $p < 0.001$), but negatively correlated with non-Hispanic Black ($r_{tet} = -0.31$; $p < 0.001$).

Table 5. Weighted correlations ($n_{unweighted}$ = 2,939)

	1	2	3	4	5	6	7	8	9	10	11
1 Age	1.00										
2 Male	0.04	1.00									
3 Education level	-0.03	0.34*	1.00								
4 NH White	0.25*	0.34*	0.29*	1.00							
5 NH Black	-0.16*	-0.40*	-0.32*	-0.98*	1.00						
6 NH Other	-0.09*	0.01	0.04	-0.68*	-0.84*	1.00					
7 Hispanic/Latinx	-0.02	0.26*	0.12*	-0.82*	-0.94*	-0.60*	1.00				
8 Anxiety symptoms	-0.07*	-0.07*	-0.08*	0.05	-0.08*	0.13*	-0.02	1.00			
9 Depression symptoms	-0.04	-0.08*	-0.10*	0.02	-0.02	0.05	-0.01	0.71*	1.00		
10 HIV stigma score	-0.09*	-0.25*	-0.11*	-0.06*	0.07*	0.07	-0.08*	0.30*	0.31*	1.00	
11 Ever IDU	0.11*	0.18*	0.03	0.29*	-0.31*	0.16	0.01	0.13*	0.11*	-0.01	1.00

*$p < 0.05$. IDU = intravenous drug use. NH = non-Hispanic.

CFA for Syndemic Burden

Results for the initial syndemic burden model indicated a suitable fit ($\chi^2 = 498.72$, $p < 0.0001$; RMSEA = 0.06; CFI = 0.90; SRMR = 0.06). Coefficients for less than a high school education vs. high school education, non-Hispanic Black vs. non-Hispanic White, and higher scores for depression and anxiety symptoms were significantly associated with higher syndemic burden (see Table 6). In contrast, male vs. female/transgender, older age, college education or higher vs. high school education, Hispanic/Latinx vs. non-Hispanic White, and ever injecting drugs were significantly associated with lower syndemic burden. Standardized results indicated being female/transgender vs. male was the largest predictor for syndemic burden (β for male = -0.52; $p < 0.001$), followed by non-Hispanic Black vs. non-Hispanic White (β = 0.44; $p < 0.001$), having high school vs. a college education (β for college = -0.38; $p < 0.001$), and HIV stigma score (β = 0.33; $p < 0.001$).

Despite a suitable fit for the data, modification indices suggested further associations between race/ethnicity and education, ever IDU, and age. The associations between race/ethnicity and education, race/ethnicity and IDU, and race/ethnicity and age were further explored and subsequently supported. First, there are inequalities in educational attainment by race/ethnicity in the U.S., with higher levels of education attained by non-Hispanic Whites, due to systemic racism in the educational system and privilege afforded to White, middle/upper-class, English-speaking students (American Psychological Association [APA], 2012). Second, the opioid epidemic likely explains racial differences in IDU, since it has historically affected non-Hispanic Whites at higher rates than other races/ethnicities (Cicero et al., 2014; Jones et al., 2015). Finally, age differences among PLWH by race/ethnicity, with non-Hispanic Whites trending older than non-Hispanic Blacks, are reflective of trends of the HIV epidemic in the U.S.

Though Blacks have been disproportionately affected by HIV since the beginning of the HIV epidemic in the U.S., the gap in incidence and prevalence rates between Blacks and Whites has widened significantly since the epidemic began in 1984 (Chapin-Bardales et al., 2017). This widening gap, in combination with most new HIV diagnoses occurring in those 25 to 29 years of age (U.S. DHHS, 2021b), results in a disproportionate number of new diagnoses among young, Black persons, bringing the average age of Black PLWH down (Sullivan et al., 2021). Correlations between race/ethnicity, education, IDU, and age variables further supported these associations (see Table 5). Therefore, residuals for indicators of race/ethnicity and education, race/ethnicity and ever IDU, and race/ethnicity and age were allowed to correlate in a respecified model.

The respecified model showed an improved fit ($\chi^2 = 311.79$, $p < 0.0001$; RMSEA = 0.06; CFI = 0.94; SRMR = 0.04). As with the initial model, coefficients for male vs. female/transgender, less than a high school education vs. high school education, college education vs. high school education, non-Hispanic Black vs. non-Hispanic White, Hispanic/Latinx vs. non-Hispanic White, depression symptoms, and anxiety symptoms were statistically significant. However, the coefficient for ever IDU became insignificant (B = 0.01; $p > 0.05$). In addition to this change, the standardized coefficient for HIV stigma became the largest indicator for syndemic burden ($\beta = 0.69$; $p < 0.001$), followed by depression symptoms ($\beta = 0.43$; $p < 0.001$), and anxiety symptoms ($\beta = 0.42$; $p < 0.001$).

Table 6. Syndemic Burden CFA ($n_{unweighted}$ = 2,939)

Syndemic burden by	Initial model		Respecified model	
	B (SE)	β (SE)	B (SE)	β (SE)
Male v. female/transgender	-0.03 (0.01)*	-0.52 (0.03)*	-0.01 (0.002)*	-0.30 (0.04)*
Less HS v. HS	0.02 (0.003)*	0.30 (0.03)*	0.004 (0.001)*	0.16 (0.04)*
Some college v. HS	-0.003 (0.002)	-0.04 (0.03)	0.000 (0.001)	-0.002 (0.03)
College v. HS	-0.02 (0.004)*	-0.38 (0.04)*	-0.01 (0.001)*	-0.18 (0.04)*
NH Black v. NH white	0.03 (0.01)*	0.44 (0.05)*	0.003 (0.001)*	0.10 (0.04)*
NH Other v. NH white	0.000 (0.001)	0.02 (0.04)	0.001 (0.001)	0.06 (0.03)
Hispanic v. NH white	-0.01 (0.002)*	-0.19 (0.03)*	-0.002 (0.001)*	-0.08 (0.03)*
Age (years)	-0.25 (0.08)*	-0.14 (0.04)*	-0.10 (0.03)*	-0.11 (0.03)*
Ever IDU v. no IDU	-0.01 (0.002)*	-0.12 (0.04)*	0.000 (0.001)	0.01 (0.03)
Depression score	0.15 (0.02)*	0.20 (0.05)*	0.16 (0.02)*	0.43 (0.03)*
Anxiety score	0.12 (0.03)*	0.16 (0.05)*	0.15 (0.02)*	0.42 (0.03)*
HIV stigma score	RI	0.33 (0.05)*	RI	0.69 (0.05)*

Note. B = unstandardized coefficient. β = standardized coefficient. HIV = human immunodeficiency virus. HS = high school. IDU = intravenous drug use. NH = non-Hispanic. RI = referent indicator. SE = standard error.

*$p < 0.05$.

Discussion

HIV stigma, depression symptoms, and anxiety symptoms were the largest predictors for syndemic burden. Previous research that included HIV stigma as a syndemic factor has shown high associations between greater levels of stigma, poorer mental health, and greater syndemic burden. For instance, McMahon et al. (2019) examined the cross-sectional associations between the syndemic factors of HIV, substance use dependence, mental health, HIV stigma, social support, and demographic characteristics with ART adherence and viral load among heterosexual men using a SEM. Results of that study showed an association between higher levels of anxiety and higher levels of HIV stigma. Further, anxiety mediated the relationship between greater levels of HIV stigma and lower rates of ART adherence (McMahon et al., 2019). Another study by Tsuyuki et al. (2017) used CFA to assess differences in the syndemic effects of substance use disorder, violence, and mental health among heterosexual men, heterosexual women, and MSM living with HIV. The authors found anxiety, depression, and substance use were significant indicators for the syndemic of substance use disorder, violence, and mental health among

PLWH. These factors, however, differed by gender and sexual orientation. Heterosexual men and MSM showed greater parameter estimates for anxiety and depression than heterosexual women while heterosexual women showed greater parameter estimates for substance use disorder than heterosexual men and MSM (Tsuyuki et al., 2017). The current study, which also found high associations between HIV stigma, anxiety symptoms, depression symptoms, and syndemic burden, supports the results from these two studies in a more diverse and representative Southern population. Further, the current study expanded on the results of these studies by focusing on those ever-injecting drugs, rather than on general substance use disorders.

In addition to stigma and mental health, the current study found female/transgender, less than high school education, and non-Hispanic Black race/ethnicity were all associated with higher levels of syndemic burden. Previous studies on associations between these factors support these results. For instance, mental health conditions such as depression and anxiety are more prevalent among women living with HIV than men living with HIV who inject drugs (Genberg et al., 2019; Robinson & Knowlton, 2016; Wisniewski et al., 2005). Other studies have found those with less than a high school education have higher levels of HIV stigma and greater prevalence of depression compared to those with a high school education or more (Illangasekare et al., 2013; Wolitski et al., 2009). Finally, non-Hispanic Black MSM living with HIV have been found to have a greater number of syndemic conditions than non-Hispanic White MSM living with HIV (Friedman et al., 2015). This high syndemic burden among non-Hispanic Blacks may be associated with systemic racism and the intersecting stigmas of HIV, race, and sexual orientation, depression, substance use, and poverty (Quinn et al., 2018). However, more research on factors associated with high syndemic burden among non-Hispanic Black PLWH and

mechanisms behind their influence is needed to increase our understanding of syndemic burden and ultimately inform interventions on reducing this burden.

A notable outcome from this study is that ever IDU became a non-statistically significant factor for syndemic burden after model respecification allowed residuals for race/ethnicity and ever IDU, education level, and age to correlate. Since not allowing residuals of related variables to correlate can result in overestimation of parameters (Reddy, 1992), this result indicates that the association of ever IDU with syndemic burden may be overestimated when the relationships between race/ethnicity, IDU, education, and age are not considered. Despite ever IDU becoming a non-significant indicator of syndemic burden in this study, it should be noted there may be differences in syndemic factors between those who are currently injecting drugs and those who are no longer injecting drugs, i.e., those in recovery. For instance, people in recovery with strong social, spiritual, or religious support have greater success in abstaining from drug use and higher quality of mental health (Avants et al., 2001; Durvasula & Miller, 2014; Préau et al., 2007). In contrast, depression and emotional pain suppress resilience in PWID (Stajduhar et al., 2009). In the current study, only 20.7% of those reporting ever IDU also reported injecting in the past 12 months, suggesting most of those ever-injecting drugs were in recovery. Therefore, resiliency and social support associated with being in recovery may have contributed to ever IDU becoming an insignificant indicator for syndemic burden in this study. Future research on differences in factors associated with syndemic burden between PLWH currently injecting drugs and those in recovery is needed to better understand what about recovery may reduce the association between IDU and syndemic burden.

Limitations of this study include those inherent in survey research, secondary data analysis, and cross-sectional analysis. Intravenous drug use was based on self-report and

therefore may have response bias. Though the HIV stigma scale, GAD-7, and PHQ-8 scales have been previously validated (Kroenke et al., 2009; Spitzer et al., 2006; Wright et al., 2007), they may also have response bias. In addition, the cross-sectional nature of this analysis does not allow for any causal interpretation of results. Finally, though the model for syndemic burden is based on theory and previous research, there is a risk for confirmation bias. Other valid alternative models for syndemic burden may exist.

This study shows the feasibility and construct validity of a theoretical model for the syndemic burden of intravenous drug use, mental health, and HIV stigma. The high association between HIV stigma, depression symptoms, and anxiety symptoms with syndemic burden indicate these factors could be targets for intervention. However, to validate these factors as targets for intervention, future research should identify and assess potential mechanisms between these factors and syndemic burden. In addition, results of this study generated questions about additional factors that may influence syndemic burden to be investigated moving forward, such as current vs. former drug use and systemic racism. Finally, research should continue to investigate the effects of syndemic burden on health outcomes, including HIV care engagement, substance use treatment, and mental health care, with the ultimate goal of improving health outcomes among PWID/LWH.

CHAPTER V: ASSOCIATION BETWEEN HIV CARE AND COVERAGE AND THE SYNDEMIC BURDEN OF INTRAVENOUS DRUG USE, MENTAL HEALTH, AND HIV STIGMA

Abstract

People who inject drugs and are living with HIV (PWID/LWH) have low rates of HIV care engagement due to multiple health-related and social conditions. Syndemic theory provides a framework to better understand the complex interaction of affiliated conditions and their associations with HIV care. This study assessed the relationship between HIV care and coverage and the syndemic burden of intravenous drug use (IDU), mental health, and HIV stigma using structural equation modeling. A previously validated measurement model for syndemic burden included indicators for HIV stigma, mental health, IDU, gender, education level, race/ethnicity, and age. A newly developed measurement model for HIV care and coverage, which included indicators for care retention, ART adherence, viral suppression, and insurance coverage, was tested and validated. The resulting association between the two models indicated a statistically significant negative correlation between HIV care and coverage and syndemic burden, with HIV stigma, HIV care retention, and mental health contributing the greatest effects on the model. The results of this study indicate HIV stigma and mental health may be targets for intervention to improve HIV care engagement.

Key Words: HIV, syndemic, stigma, substance use, mental health, HIV care engagement

Introduction

Initial linkage to and ongoing engagement in HIV medical care among people living with HIV (PLWH) are challenging but vital components of the Ending the HIV Epidemic plan in the United States (United States Department of Health and Human Services [U.S. DHHS], 2019). However, there are inequities in HIV care engagement. For instance, people who inject drugs and are living with HIV (PWID/LWH) are less likely to be linked and retained in HIV care than PLWH who do not inject drugs (Fleishman et al., 2012; Lesko et al., 2017; Westergaard et al., 2013). PWID/LWH are also less likely to be prescribed or receive ART, adhere to ART regimens, and be virally suppressed than PLWH who do not inject drugs (Chander et al., 2006; Himelhoch et al., 2007; Lesko et al., 2017; McGowan et al., 2011; Mizuno et al., 2015; Morris et al., 2007; Westergaard et al., 2012, 2013). Factors associated with non-adherence among PWID/LWH include social conditions (e.g., younger age, female sex, lower levels of education, and minority race/ethnicity) and health-related factors (e.g., poor physical health, ART-related beliefs, high-risk sexual behaviors, and needle sharing) (Bazzi et al., 2019). In addition, several studies have identified mental health conditions as being associated with poor ART adherence and low rates of viral suppression among PWID/LWH (Bazzi et al., 2019; Blashill et al., 2014; Himelhoch et al., 2007; Mizuno et al., 2015; Robinson & Knowlton, 2016; Waldrop-Valverde & Valverde, 2005). This association is particularly concerning due to the high prevalence of comorbid mental health conditions in PWID/LWH (Jones et al., 2010; Wisniewski et al., 2005). Further, the interaction of drug use, poor mental health, and social conditions associated with poorer health outcomes can exacerbate this association, since PWID/LWH with more co-occurring psychosocial conditions (i.e., polydrug use, childhood abuse, psychological distress,

low social support, homelessness, and incarceration) have lower odds of ART adherence or viral suppression than those with none of these conditions (Mizuno et al., 2015).

Further complicating the association between drug use, mental health, and HIV care is stigma. Stigma experienced by PWID/LWH, whether due to their HIV diagnosis or drug use, can worsen mental health conditions such as depression. Though not specific to PWID/LWH, a study of PLWH with a history of substance use found a significant association between HIV stigma, drug use stigma, and depression, with those experiencing both types of stigma having even higher levels of depression (Earnshaw et al., 2015). The effect of stigma and depression, along with drug use, is further associated with lower HIV care engagement. For instance, a study on Black and Hispanic/Latinx people living with HIV for 10 years or more found interactions between stigma, substance use, low social support, poor housing quality, and depression all contributed to ART non-persistence (Gwadz et al., 2021). Notably, that study also found IDU was associated with sustained ART adherence. However, the authors contributed this result to the length of time since diagnosis (at least 10 years) and experience managing ART in the sample (Gwadz et al., 2021).

The complexity of the associations between drug use, mental health, stigma, and HIV care suggests these factors do not contribute to poor outcomes in isolation. This concept of interacting components influencing health outcomes is supported by syndemic theory (Singer & Clair, 2003). The term *syndemic* was first applied to HIV/AIDS by Merrill Singer to explain disparities in AIDS outcomes among urban, poor people of color (Singer, 1994). Since then, the syndemic framework has been used extensively in HIV research, particularly for understanding relationships between HIV and substance use (González-Guarda et al., 2011; Perlman & Jordan, 2018; Robinson et al., 2016; Singer, 1994, 1996). However, many studies on syndemic burden in

PLWH do not specifically include PWID/LWH. In addition, due to the difficulty of engaging PWID/LWH in research, studies which do include this population often have limited, less representative samples. Further, HIV care engagement is often measured using one construct at a time (e.g., ART adherence or viral suppression). However, HIV care is a complex concept with multiple influences and dimensions. For instance, the HIV care continuum, the treatment pathway for PWLH, has multiple stages: diagnosis, linkage to care, retention in care, ART receipt and adherence, and viral suppression. Notably, PLWH frequently go back and forth between each stage, making this continuum more like a cascade than a step-by-step process, with PLWH falling into higher or lower levels of care engagement (Mugavero, 2016). Adding to the complexity, engagement in the HIV care continuum is influenced by multiple factors, such as the syndemic factors discussed above and socioeconomic factors such as insurance coverage (Kates et al., 2021; Ludema et al., 2016).

Accordingly, the current study uses a diverse, representative sample of PLWH, which includes PWID/LWH, from the Centers for Disease Control and Prevention's (CDC) Medical Monitoring Project (MMP). In addition, the current study conceptualizes HIV care and coverage as a latent construct consisting of multiple aspects of HIV care and management—care retention, ART adherence, viral suppression, and insurance coverage. The overall purpose of this study is to 1) test the construct validity of a measurement model for the concept of HIV care and coverage and 2) assess the association between the syndemic burden of IDU, mental health, and HIV stigma with HIV care and coverage.

Materials and Methods

Data Source and Measures

Data for this analysis are from CDC's MMP, an annual, nationally representative survey of adults living with HIV in the U.S. MMP has complemented the National HIV Surveillance System (NHSS), which collects core characteristics of all PLWH in the U.S. and its territories, by collecting more detailed information on clinical outcomes, HIV care engagement, and health behaviors (CDC, 2015). This analysis uses data from 2015 through the latest year of available data (2018 or 2019) from three Southern U.S. states. Southern states were selected for this study because the Southern U.S. has the highest number of PLWH compared to other regions of the country with over 460,000 in 2018 (CDC, 2021b). The Southern U.S. also has the highest proportion of new HIV cases, with 51% of all new U.S. cases in 2018 occurring in the South (CDC, 2022b). The three states included in this study are Florida, Georgia, and Virginia.

Syndemic burden for intravenous drug use, mental health, and HIV stigma was assessed using a previously identified measurement model (see Chapter 4). Briefly, a latent variable for syndemic burden was manifested through indicators for health-related factors (i.e., ever IDU, depression symptoms, and anxiety symptoms) and social conditions (i.e., HIV stigma, gender, education, race/ethnicity, age). Ever IDU was determined by asking participants whether they had ever injected drugs or had someone else inject them with drugs not for medical purposes. Depression and anxiety symptoms were measured using the Personal Health Questionnaire (PHQ)-8 and General Anxiety Disorder (GAD)-7, respectively (Kroenke et al., 2009; Spitzer et al., 2006). A modified version of the HIV stigma scale was used to assess stigma (Wright et al., 2007). Cultural positionality was measured using gender (male, female/transgender), education level (less than high school, high school, some college, college degree or higher), race/ethnicity

(non-Hispanic White, non-Hispanic Black, noon-Hispanic Other, Hispanic/Latinx), and age (in years). Female and transgender persons were combined into a single referent variable due to the small sample of transgender persons (n = 30).

HIV care indicators included care retention, ART adherence, viral suppression, and employer-sponsored insurance coverage status. Care retention was self-reported as not having any missed HIV-related appointments in the past 12 months. ART adherence was defined as the self-reported percentage of days with no missed doses over the past 30-days ([30 - number of days with missed doses] / 30 * 100). Viral suppression was defined as a viral load <200 copies/mL blood at the most recent viral load test in the medical record. Insurance type was divided into two categories: employer-sponsored insurance or no employer-sponsored insurance. Insurance coverage was included in the model since it has previously been associated with higher levels of HIV care engagement despite robust safety net programs for PLWH, such as the Ryan White HIV/AIDS Program (Holtzman et al., 2015; Sangaramoorthy et al., 2021; Yehia et al., 2015). Participants reporting any private insurance coverage or coverage through the U.S. Department of Defense Military Health System (i.e., TRICARE) were considered to have employer-sponsored insurance. Those not reporting either of these types of insurance were placed into the no employer-sponsored insurance category.

HIV Care and Coverage CFA

The construct validity of a latent variable for HIV care and coverage was assessed using CFA. The concept of HIV care is often measured using individual measures of the HIV care continuum. For instance, many studies utilize ART adherence or viral load as proxy measures for the concept of HIV care. However, using a latent variable for the concept of HIV care and coverage, which includes stages of the HIV care continuum and insurance coverage, more

accurately portrays the true complexity of this concept. Since CFA calculates all coefficients at once, instead of one at a time as in multiple regression, it accounts for the variances of all included indicators to address any potential interdependence of HIV care measures (i.e., care retention, ART adherence, and viral suppression) (Beran & Violato, 2010). Further, since they are not directly observed, latent variables help eliminate measurement errors associated with assessing each care indicator individually (Lei & Wu, 2007). The model was identified by scaling the latent variable (i.e., HIV care and coverage) to ART adherence. Scaling the latent variable identifies the model and allows parameters to be estimated. ART adherence was chosen as the referent indicator since it was the only continuous indicator for HIV care and coverage. The resulting HIV care and coverage model was then used in the structural model.

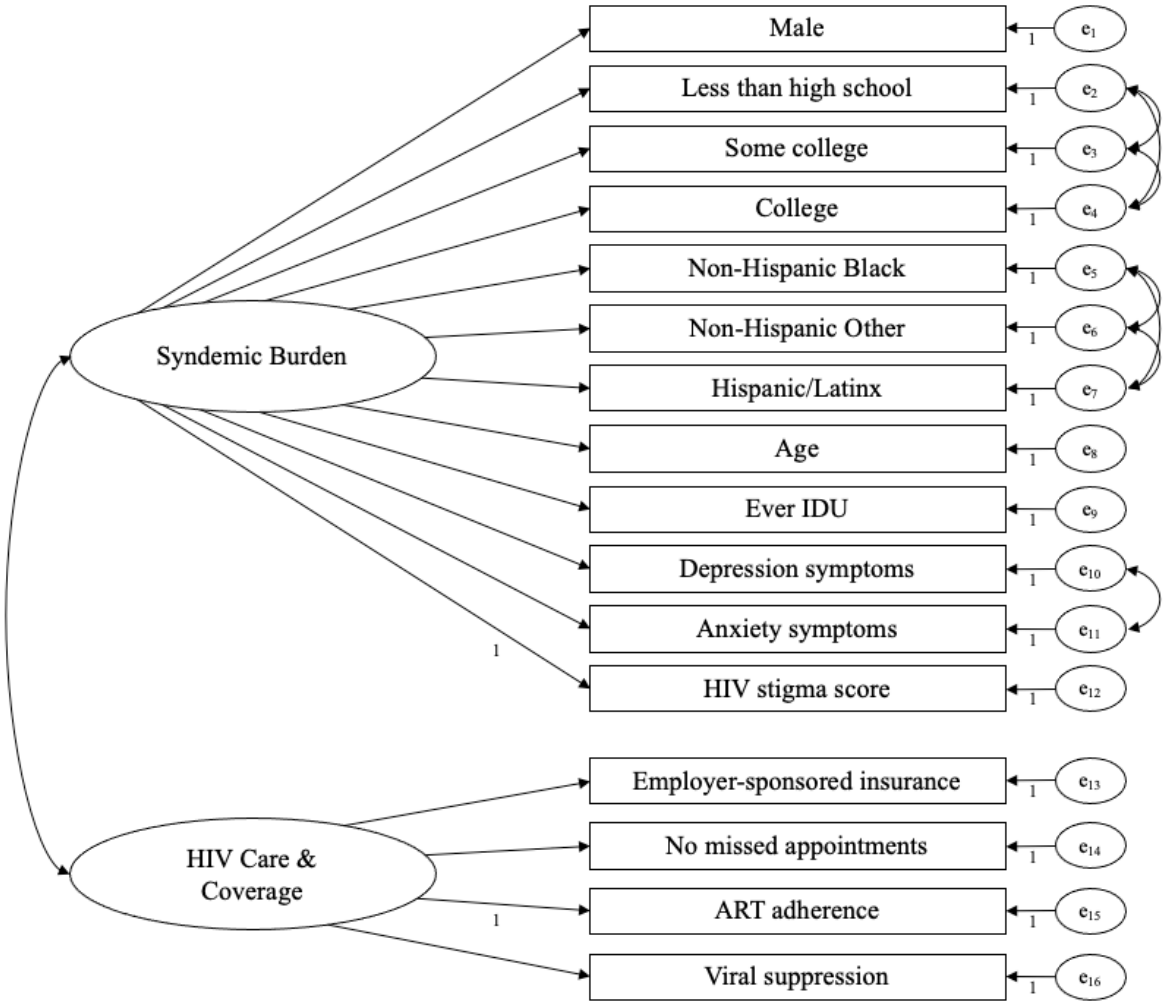
Syndemic Burden and HIV Care and Coverage SEM

The previously established measurement model for syndemic burden and the newly constructed measurement model for HIV care and coverage were included in the SEM to assess the association between the two constructs (see Figure 7). The latent variable for syndemic burden was scaled to HIV stigma score. Residuals in the syndemic burden model were allowed to correlate between indicators of the categorical variables of which they are from (e.g., less than high school, some college, and college) to adjust for the resulting correlation between them. In addition, due to high correlation between depression and anxiety, the residuals for these variables were also allowed to correlate. Finally, the residuals of indicators for race/ethnicity and education, race/ethnicity and IDU, and race/ethnicity and age were allowed to correlate due to the strong correlations and known relationships between them. In the U.S., there are racial inequities in educational attainment, with non-Hispanic White students having greater access to higher education (American Psychological Association [APA], 2012). Non-Hispanic Whites are

also more likely to report IDU, reflecting the characteristics of the opioid epidemic which disproportionately affects non-Hispanic Whites (Cicero et al., 2014; Jones et al., 2015). Finally, greater HIV incidence among young, non-Hispanic Black persons compared to non-Hispanic White persons has skewed the average age for Black PLWH to be younger than that of White PLWH (Chapin-Bardales et al., 2017; Sullivan et al., 2021; U.S. DHHS, 2021b).

The association between the two latent variables for syndemic burden and HIV care and coverage was represented by a curved, double-headed arrow to show covariance between them.

Figure 7. Proposed SEM for Syndemic Burden and HIV Care and Coverage



Note. Syndemic burden is manifested through indicators for gender (ref. female/transgender), education (ref. high school), race/ethnicity (ref. non-Hispanic White), age, IDU status (ref. never injected drugs), mental health, and HIV stigma. HIV care and coverage is manifested through insurance, care retention, ART adherence, and viral suppression. The arrow between syndemic burden and HIV care and coverage represents a correlation between them. Double-headed arrows between error terms indicate correlation between residuals. ART = antiretroviral therapy. e = error. IDU = intravenous drug use. Ref. = referent category.

Analysis

Sample characteristics were assessed using frequencies, percentages, means, and standard errors. Weighted correlations between study variables were calculated using Pearson's *r* for continuous variables, and point-biserial (r_{pb}), polychoric (r_{pc}), polyserial (r_{ps}), and tetrachoric correlations (r_{tet}) as appropriate for dichotomous, ordinal, or categorical variables.

Unstandardized and standardized parameter estimates for the CFA and SEM were calculated using maximum likelihood estimation with robust standard errors (MLR). Model fit for both CFA and SEM analyses was determined based on previously reported thresholds of good fit for RMSEA (≤0.06), CFI (≥0.90), χ^2 ($p > 0.05$), and SRMR (≤0.08) (Lei & Wu, 2007).

All analyses were weighted to account for MMP's two-stage probability sampling design, participant multiplicity, and non-response bias (Johnson et al., 2020). A *p*-value of $p < 0.05$ was considered statistically significant. All analyses were conducted using SAS v.9.4 (Cary, NC) and Mplus v.8.7 (Muthén & Muthén, 2017).

Results

The overall sample ($n_{unweighted} = 2{,}939$) was mostly male (72.4%) and non-Hispanic Black (54.4%) with an average age of 48.4 years (see Table 7). Most participants had either some college or a college degree (56.1%). In addition, most had not missed an appointment in the past 12 months (77.1%) and were virally suppressed (86.8%). Just under 9% of participants reported ever injecting drugs and 1.8% reported injecting drugs in the past 12 months.

Table 7. Sample characteristics ($n_{unweighted}$ = 2,939)

Characteristic	Unweighted *n* (weighted %) or weighted *mean ± SE*
Age (years)	48.4 ± 0.3
missing	28
State	
Florida	1,578 (60.0)
Georgia	758 (27.9)
Virginia	603 (12.1)
missing	0
Race/Ethnicity	
Non-Hispanic Black	1659 (54.4)
Non-Hispanic White	680 (25.1)
Non-Hispanic Other	173 (5.2)
Hispanic/Latinx	427 (15.4)
missing	0
Education	
Less than high school	558 (17.9)
High school	750 (26.0)
Some college	1,004 (35.0)
Bachelor's degree	608 (21.1)
missing	19
Gender	
Male	1,996 (72.4)
Female	913 (26.6)
Transgender	30 (1.0)
missing	0
Employer-sponsored insurance	
Yes	1,127 (38.5)
No	1,789 (61.5)
missing	23
Missed any appointments in past 12 months	
No	2,251 (77.1)
Yes	644 (22.9)
missing	44
% days adherent to ART over past 30 days (%)	95.4 ± 0.3
missing	182
Viral suppression (<200 copies/mL) at most recent lab test	
Yes	2,352 (86.8)
No	306 (13.2)
missing	281
Anxiety (GAD-7) score	3.3 ± 0.1
missing	38
Depression (PHQ-8) score	3.0 ± 0.1
missing	45

Table 7. Sample characteristics ($n_{unweighted}$ = 2,939), cont.

Characteristic	Unweighted *n* (weighted %) or weighted *mean ± SE*
HIV stigma score	41.1 ± 0.5
missing	131
Ever IDU	
Yes	247 (8.7)
No	2,655 (91.3)
missing	37
IDU in past 12 months	
Yes	53 (1.8)
No	2,849 (98.2)
missing	37

Note. ART = antiretroviral therapy. GAD = General Anxiety Disorder. HIV = human immunodeficiency virus. IDU = intravenous drug use. PHQ = Personal Health Questionnaire. SE = standard error.

Weighted correlations between syndemic burden and HIV care and coverage indicators showed significant correlations between higher depression symptom scores and missing an appointment (r_{pb} = 0.15; $p < 0.001$) and lower ART adherence (r = -0.07; $p < 0.001$), but not viral suppression (r_{pb} = -0.06; p = 0.12) (see Table 8). Similarly, higher anxiety symptom scores were significantly correlated with missing an appointment (r_{pb} = 0.19; p <0.001) and lower ART adherence (r = -0.13; $p < 0.001$), but not viral suppression (r_{pb} = -0.06; p = 0.09). Having employer-sponsored insurance was associated with lower depression symptom scores (r_{pb} = -0.15; $p < 0.001$), lower anxiety symptom scores (r_{pb} = -0.12; p <0.001), not missing an appointment (r_{tet} = -0.23; $p < 0.001$), and viral suppression (r_{tet} = 0.22; $p < 0.001$). Higher HIV stigma scores were correlated with missing an appointment (r_{pb} = 0.09; p = 0.003), but not ART adherence (r = -0.03; p = 0.14) or viral suppression (r_{pb} = -0.02; p = 0.57). Finally, non-Hispanic White race/ethnicity was significantly correlated with not missing an appointment (r_{tet} = -0.17; p <0.001), higher ART adherence (r_{pb} = 0.17; $p < 0.001$), and viral suppression (r_{tet} = 0.22; $p <$ 0.001) and non-Hispanic Black race/ethnicity was significantly correlated with missing an appointment (r_{tet} = 0.12; p = 0.003), lower ART adherence (r_{pb} = -0.07; p = 0.02), and no viral suppression (r_{tet} = -0.21; $p < 0.001$).

Table 8. Weighted Correlations ($n_{unweighted}$ = 2,939)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1 Age	1.00														
2 Male	0.04	1.00													
3 Education level	-0.03	0.34*	1.00												
4 NH White	0.25*	0.34*	0.29*	1.00											
5 NH Black	-0.16*	-0.40*	-0.32*	-0.98*	1.00										
6 NH Other	-0.09*	0.01	0.04	-0.68*	-0.84*	1.00									
7 Hispanic/ Latinx	-0.02	0.26*	0.12*	-0.82*	-0.94*	-0.60*	1.00								
8 Anxiety symptoms	-0.07*	-0.07*	-0.08*	0.05	-0.08*	0.13*	-0.02	1.00							
9 Depression symptoms	-0.04	-0.08*	-0.10*	0.02	-0.02	0.05	-0.01	0.71*	1.00						
10 HIV stigma	-0.09*	-0.25*	-0.11*	-0.06*	0.07*	0.07	-0.08*	0.30*	0.31*	1.00					
11 Ever IDU	0.11*	0.18*	0.03	0.29*	-0.31*	0.16	0.01	0.13*	0.11*	-0.01	1.00				
12 Missed appt.	-0.21*	-0.09*	-0.15*	-0.17*	0.12*	-0.01	0.03	0.19*	0.15*	0.09*	0.05	1.00			
13 ART adh.	0.10*	0.02	-0.01	0.17*	-0.07*	-0.09	0.01	-0.13*	-0.07*	-0.03	-0.05	-0.24*	1.00		
14 Viral supp.	0.21*	0.05	0.16*	0.22*	-0.21*	0.07	0.05	-0.06	-0.06	-0.02	-0.05	-0.28*	0.18*	1.00	
15 Employer ins.	-0.09*	0.24*	0.44*	0.20*	-0.14*	0.02	-0.05	-0.12*	-0.15*	-0.03	-0.09	-0.23*	0.06	0.22*	1.00

Note. Appt. = appointment. ART adh. = antiretroviral therapy adherence. IDU = intravenous drug use. Ins. = Insurance. NH = non=Hispanic. Supp. = suppression.

*$p < 0.05$.

HIV Care and Coverage CFA

Results of the HIV care and coverage CFA indicated the data were a good fit for the model (RMSEA = 0.04; CFI = 0.93; $\chi^2 = 10.92$, $p = 0.004$; SRMR = 0.02). Standardized results showed that not missing an appointment in the past 12 months was the strongest indicator of HIV care and coverage (β = 0.49), followed by ART adherence (β = 0.43), viral suppression (β = 0.34), and insurance coverage (β = 0.22) (all $p < 0.001$) (see Table 9).

Table 9. CFA for HIV Care and Coverage ($n_{unweighted}$ = 2,936)

Care and coverage by	Unstandardized model		Standardized model	
	B (SE)	*p*-value for B	β (SE)	*p*-value for β
ART adherence (% days adherent over past 30-days)	RI	RI	0.43 (0.06)	<0.001
Viral suppression v. no viral suppression	2.19 (0.51)	<0.001	0.34 (0.07)	<0.001
No missed appointments v. missed appointments in past 12 months	3.88 (0.92)	<0.001	0.49 (0.07)	<0.001
Employer-sponsored insurance v. no employer-sponsored insurance	2.03 (0.56)	<0.001	0.22 (0.04)	<0.001

Note. Viral suppression defined as <200 copies HIV/mL blood at most recent test. ART = antiretroviral therapy. B = unstandardized coefficient. β = standardized coefficient. RI = referent indicator. SE = standard error.

Syndemic Burden and HIV Care and Coverage SEM

The resulting correlation between syndemic burden and HIV care and coverage indicated a significant negative association between the two constructs ($r = -0.47$; $p < 0.001$) (see Initial Model column in Table 10). Although the initial SEM produced a sufficient model fit (RMSEA = 0.05; CFI = 0.86; $\chi^2 = 715.79$, $p < 0.0001$; SRMR = 0.05), potential improvement in fit was explored. Modification indices indicated association between insurance type and level of education. Since education level is often directly associated with employment, and therefore employment-sponsored insurance coverage in the U.S., this was not surprising. Correlations and covariances between the education and insurance variables supported this association (see Table

8). Therefore, respecification of the model allowed the residuals of the education and insurance indicators to correlate.

The respecified model showed improved fit (RMSEA = 0.04; CFI = 0.90; $\chi^2 = 524.00$, $p < 0.0001$; SRMR = 0.05). The correlation between syndemic burden and HIV care and coverage decreased but was still significant ($r = -0.39$; $p < 0.001$) (see Respecified Model columns in Table 10).

Table 10. SEM for Syndemic Burden and HIV Care and Coverage ($n_{unweighted}$ = 2,939)

	Initial model		Respecified model	
	B (SE)	β (SE)	B (SE)	β (SE)
Syndemic burden by				
Male v. female/transgender	-0.01 (0.004)*	-0.34 (0.07)*	-0.01 (0.002)*	-0.31 (0.05)*
Less than high school v. high school	0.01 (0.003)*	0.21 (0.06)*	0.01 (0.001)*	0.17 (0.04)*
Some college v. high school	0.000 (0.001)	0.004 (0.03)	0.000 (0.001)	0.01 (0.03)
College v. high school	-0.01 (0.003)*	-0.27 (0.06)*	-0.01 (0.001)*	-0.22 (0.04)*
Non-Hispanic Black v. non-Hispanic white	0.01 (0.004)	0.15 (0.07)*	0.01 (0.002)*	0.14 (0.05)*
Non-Hispanic Other v. non-Hispanic white	0.001 (0.001)	0.07 (0.04)	0.001 (0.001)	0.07 (0.04)
Hispanic/Latinx v. non-Hispanic white	-0.003 (0.001)*	-0.09 (0.04)*	-0.002 (0.001)*	-0.09 (0.03)*
Age (years)	-0.16 (0.04)*	-0.15 (0.03)*	-0.16 (0.04)*	-0.16 (0.03)*
Ever IDU v. never IDU	0.001 (0.001)	0.02 (0.04)	0.000 (0.001)	0.02 (0.04)
Depression (PHQ-8) score	0.21 (0.02)*	0.45 (0.06)*	0.20 (0.02)*	0.46 (0.04)*
Anxiety (GAD-7) score	0.21 (0.02)*	0.45 (0.07)*	0.20 (0.02)*	0.46 (0.05)*
HIV stigma score	RI	0.54 (0.07)*	RI	0.59 (0.04)*
HIV care and coverage by				
ART adherence (% days adherent over past 30-days)	RI	0.38 (0.05)*	RI	0.41 (0.04)*
Viral suppression v. no viral suppression	2.31 (0.46)*	0.31 (0.05)*	2.11 (0.40)*	0.31 (0.05)*
No missed appointments v. missed appointments in past 12 months	4.55 (0.70)*	0.50 (0.06)*	4.26 (0.77)*	0.51 (0.06)*
Employer-sponsored insurance v. no employer-sponsored insurance	3.01 (1.00)*	0.28 (0.06)*	2.17 (0.51)*	0.23 (0.04)*
Syndemic burden with HIV care and coverage	-0.25 (0.04)*	-0.47 (0.12)*	-0.25 (0.04)*	-0.39 (0.08)*

Note. Viral suppression defined as <200 copies HIV/mL blood at most recent test. ART = antiretroviral therapy. B = unstandardized coefficient. β = standardized coefficient. GAD = General Anxiety Disorder. HIV = human immunodeficiency virus. IDU = intravenous drug use. PHQ = Personal Health Questionnaire. RI = referent indicator. SE = standard error.

*$p < 0.05$.

Discussion

The results of this study show a statistically significant negative correlation between HIV care and coverage and syndemic burden among PLWH. In other words, as syndemic burden increased, HIV care and coverage decreased (and vice versa). These results support previous studies on the association between greater syndemic burden and lower HIV care engagement. For instance, a study on the syndemic of Substance Use, Mental Illness, and Familial Conflict non-negotiation (SUMIC) among Black PWID found those with high levels of substance use and mental health conditions were less likely to be virally suppressed than those with moderate substance use and mental health conditions, high mental health conditions alone, or moderate substance use and high familial conflict non-negotiation (Robinson et al., 2016). Other studies on syndemic burden have found PLWH experiencing more syndemic conditions are less likely to be retained in care, adherent to ART, and virally suppressed than those with fewer or no syndemic conditions (Blashill et al., 2015; Friedman et al., 2015; Glynn et al., 2019; Kuhns et al., 2016; Mizuno et al., 2015; Satyanarayana et al., 2021). The largest predictor for this association in the current study was HIV stigma. The effect of HIV stigma on HIV care engagement is supported by a study by McMahon et al. (2019), which found higher levels of stigma to be associated with higher levels of anxiety, which in turn was associated with lower ART adherence.

Due to previous studies showing a relationship between substance use, syndemic burden, and HIV care, the non-statistically significant contribution of ever IDU on the association between syndemic burden and HIV care and coverage in the current study was not expected. Of the 247 PLWH reporting ever injecting drugs in the current study, 20.7% reported injecting in the past 12 months. In this study, it is not clear what proportion of those who reported ever injecting drugs but not injecting in the past 12 months were in recovery from a substance use

disorder and what proportion had been recreational users of injection drugs. However, previous studies have shown over half of people who have ever injected drugs meet the criteria for substance use disorder (Hartzler et al., 2017; Martins et al., 2017; Novak & Kral, 2011), which may suggest most of those ever-injecting drugs in the current study were in recovery from a substance use disorder. Therefore, being in recovery may be associated with lower syndemic burden or higher HIV care and coverage. Other studies support differences in HIV care among PWID/LWH. For instance, those who were no longer injecting drugs were more likely to receive ART from a provider than those currently injecting (Wagman et al., 2020). Recovery may be associated with improved HIV care due to factors associated with it, such as higher levels of social support. For example, one study found the increased social support associated with being in recovery likely attenuates the association of drug dependence severity on ART adherence (McMahon et al., 2019). In other words, having support from family and friends reduces the burden of substance dependence.

In addition to assessing the association between syndemic burden and HIV care and coverage, this study validated a measurement model of HIV care and coverage using indicators for care retention, ART adherence, viral suppression, and insurance. Interestingly the order of the influence of indicators on HIV care and coverage mirrors the temporal order of the HIV care continuum (Mugavero, 2016), with care retention being the largest predictor, followed by ART adherence and viral suppression. While still significant, employer-sponsored insurance was the least influential indicator. This result may reflect success of interventions to increase access to HIV care, such as patient navigation programs or the Ryan White HIV/AIDS program (HIV Prevention Research Synthesis Project, 2022; Mandsager et al., 2018). However, its statistical significance may indicate that despite good progress in the U.S., HIV care is still associated with

the type of insurance one has. Some research has shown having employer-sponsored insurance increases access to providers and the ability to pay for care and prescriptions (Holtzman et al., 2015; Sangaramoorthy et al., 2021; Yehia et al., 2015). Notably, states which have expanded Medicaid under the Affordable Care Act have seen improvement in access to and ability to pay for HIV care (McManus et al., 2021a, 2021b; Wade et al., 2020). As of the time of data collection for this study, none of the included states had implemented Medicaid expansion. Therefore, the significance of having employer-sponsored insurance in the included states may be more impactful than among states which have expanded Medicaid.

This study is not without limitations. The data for this study are from three Southern states, limiting the generalizability to the entire U.S. or other countries. In addition, it was assumed, though not known, in the interpretation of results that those reporting ever injecting but not injecting in the past 12 months were in recovery. The validity of this study may also be threatened by biases inherent to cross-sectional survey research and SEM methods. First, the negative correlation between syndemic burden and HIV care and coverage is a measure of how much these two variables are linearly associated; however, this relationship may not be linear. Therefore, this correlation may underestimate the relationship between these two factors. Second, since MMP surveys were conducted cross-sectionally, results of this analysis cannot be used to infer causality. Also, though validated measures were utilized by MMP (e.g., PHQ-8), no measure can perfectly assess psychosocial constructs. In addition, some measures were self-reported (e.g., number of days with missed doses of ART), which may be affected by response bias (e.g., recall or social-desirability biases). Viral load was determined based on the most recent value in the medical record; however, the time between lab results and completing the MMP interview varied. Finally, the SEM used in this study is based on theory and supported by

previous research; however, there is a risk for confirmation bias since there could be valid, alternative models that were not tested. Omission of constructs relevant to the analysis and/or omission of any factor that could be an alternative explanation for an association may result in specification errors and/or confounding.

Overall, this study found greater syndemic burden was associated with lower levels of HIV care and coverage among PLWH in the Southern U.S. The largest indicators for this association were HIV stigma, depression symptoms, and anxiety symptoms. These factors may therefore be targets for intervention to increase HIV treatment and care engagement. In addition, the significance of social determinants of health (i.e., race/ethnicity, gender, age, and educational level) in the model may indicate these factors should be either considered as part of an intervention or as points for systemic intervention (e.g., policies to address racism, sexism, and/or inequities in education). Other studies that have explored associations between HIV stigma, mental health, social determinants of health, and HIV care outcomes have found the interaction of these conditions have negative impacts on ART adherence (Gwadz et al., 2021; Quinn et al., 2018). Addressing social determinants of health is therefore a vital component of addressing the HIV epidemic. Finally, more research should focus specifically on those currently injecting drugs and/or those in recovery to assess differences in syndemic burden and HIV care by recovery status and explore aspects associated with recovery (e.g., social support, resilience) that may reduce syndemic burden or improve HIV care.

CHAPTER VI: DISCUSSION AND IMPLICATIONS

As a scientist, my goal is to improve society and people's everyday lives through uncovering facts. While using theory helps us piece together related facts to uncover a more complete picture of an issue, there are many different ways to interpret them collectively. Everyone has their own reality and experiences that may not align with a generalized interpretation of an issue or one specific theory. This is especially true when we examine complex issues such as drug use, mental health, and stigma. In addition to my position as a scientist, my cultural positionality as a white, cis-gender female in higher education affords me privileges and experiences that influence my interpretations. Because of this, results of this study should be taken in context of others' experiences and research in these areas.

The overall purpose of this dissertation was to evaluate the association between HIV care and coverage and the syndemic burden of IDU, mental health, and HIV stigma. To achieve this purpose, the aims of this study also included assessing the construct validity of a theoretical model of syndemic burden as well as for a model of HIV care and coverage:

- Aim 1: Assess the construct validity of a theoretical model of the syndemic burden of mental health, IDU, and HIV stigma
- Aim 2: Assess the construct validity of a theoretical model for HIV care and coverage
- Aim 3: Evaluate the direction and extent of the association between the syndemic burden of mental health, IDU, and HIV stigma and HIV care and coverage

A syndemic is a phenomenon of interrelated and mutually reinforcing health and social factors (Singer, 1994, 1996). Syndemic theory is therefore a useful lens for better understanding the multiple health and social factors experienced by PWID/LWH, including drug use, mental health conditions, and stigma, and the ways in which they interact to affect health-related outcomes. Because it addresses the complexity of multiple health and social factors often

experienced by PWID/LWH, using syndemic theory to study HIV may better address the lived realities of PWID/LWH and help us identify more appropriate and effective interventions to improve HIV care. Accordingly, this study demonstrated the construct validity of a theoretical model of syndemic burden, which included indicators for health-related conditions (IDU and mental health) and social conditions (gender, education level, race/ethnicity, age, and HIV stigma). Significant predictors for higher levels of syndemic burden included female/transgender, non-Hispanic Black race/ethnicity, less than high school education, higher HIV stigma scores, and higher levels of depression and anxiety symptoms. Previous studies have found similar associations. For instance, mental health conditions such as depression and anxiety are more prevalent among women living with HIV than men (Genberg et al., 2019; Robinson & Knowlton, 2016; Wisniewski et al., 2005), non-Hispanic Black MSM living with HIV have a greater number of syndemic conditions than non-Hispanic White MSM living with HIV (Friedman et al., 2015) and those with less than a high school education have higher levels of HIV stigma and depression compared to those with a high school education or more (Illangasekare et al., 2013; Wolitski et al., 2009).

In contrast, lower syndemic burden was associated with having a college education, Hispanic/Latinx race/ethnicity, and older age. Higher levels of education and older age have been associated with lower social stigma and greater coping ability (Baumgartner, 2007; Reeves et al., 1999; Waite et al., 2008). Having a college education and older age may therefore be measures of resiliency. Hispanic/Latinx race/ethnicity may also be an indicator of resiliency due to the concept of familism present in many Hispanic/Latinx cultures, which prioritizes family closeness and support (González-Guarda et al., 2011).

HIV care, like syndemic burden, is a multidimensional construct. The HIV care continuum, which only addresses steps of clinical treatment, consists of five interdependent steps: diagnosis, linkage to care, retention in care, ART adherence, and viral suppression (Mugavero, 2016). However, these steps are further dependent on other factors, such as insurance coverage. In the U.S., insurance coverage is a complex measure of access to care, quality of care, and ability to pay for healthcare services and medications (Garfield et al., 2019; Institute of Medicine Committee on the Consequences of Uninsurance, 2002; Nguyen & Sommers, 2016). Therefore, this study validated a measurement model for HIV care which included indicators for HIV clinical treatment (i.e., care retention, ART adherence, and viral suppression) and insurance coverage. This approach of measuring HIV care as a multidimensional construct aligns with the field's understanding of HIV care as a continuum or cascade, where the elements are fundamentally related to and dependent on one another. In addition, assessing HIV care and coverage as a latent variable helps eliminate measurement errors associated with analyzing each care outcome separately (Lei & Wu, 2007). Results showed a good-fitting model, with all indicators as significant predictors of HIV care and coverage. Care retention was the largest indicator, followed by ART adherence, viral suppression, and employer-sponsored insurance coverage. Notably, standardized model coefficients demonstrated that the magnitude of importance for the indicators of HIV care and coverage were aligned with the temporal order of the HIV care continuum (i.e., care retention, ART adherence, and viral suppression) (Mugavero, 2016).

The inclusion of insurance status in the model was particularly novel. Results showed having employer-sponsored insurance was significantly associated with a higher level of HIV care and coverage. This result shows that despite good progress in the U.S., HIV care is still

associated with the type of insurance one has. Having employer-sponsored insurance increases access to providers and the ability to pay for care and prescriptions (Holtzman et al., 2015; Sangaramoorthy et al., 2021; Yehia et al., 2015). Therefore, including insurance status as an indicator of HIV care is important.

While having employer-sponsored insurance was significantly associated with HIV care and coverage, it should be noted that at the time of data collection (2015-2018 or 2019), none of the included states (Florida, Georgia, and Virginia) had implemented the Medicaid expansion option of the Affordable Care Act. Previous studies have generally shown improved access to HIV care among PLWH in states with Medicaid expansion (McManus et al., 2021a, 2021b; Wade et al., 2020). Similar to having employer-sponsored insurance coverage, expanding Medicaid increases access to and ability to pay for providers (McManus et al., 2021a; Wade et al., 2020). Therefore, employer-sponsored insurance may be less influential among states which have expanded Medicaid than in states that have not.

Finally, results of the SEM for syndemic burden and HIV care and coverage showed a significant negative correlation between the two constructs. This correlation indicates higher syndemic burden was associated with reduced HIV care and coverage. The largest predictors for this correlation were HIV stigma, care retention, and depression and anxiety symptoms. While the results of this study cannot be interpreted as causal, they indicate HIV stigma, depression, and anxiety could be targets for intervention. In addition, the significance of social determinants of health (i.e., race/ethnicity, gender, age, and educational level) in the model may indicate these factors should be either considered as part of an intervention or as points for systemic intervention (e.g., policies to address racism, sexism, and/or inequities in education). Other studies that have explored associations between HIV stigma, mental health, social determinants

of health, and HIV care outcomes have found the interaction of these conditions have negative impacts on ART adherence (Gwadz et al., 2021; Quinn et al., 2018). Addressing social determinants of health is therefore a vital component of addressing the HIV epidemic.

However, addressing these issues is exceptionally difficult since it requires multilevel socio-structural change. Some interventions have incorporated novel approaches to address these issues. For instance, the TransLife Care (TLC) project in Chicago, Illinois, has increased HIV care engagement by providing a multitude of services in one location to help overcome structural barriers for transgender women of color (Kuhns et al., 2021). These services include HIV case management, housing assistance, help finding employment, healthcare referrals and health education, and legal services. The authors note that a key to the success of the program is the use of community-based participation—in other words, TLC was developed *by* and *for* transgender women (Kuhns et al., 2021). Another program developed based on community-based participatory research to address structural factors contributing to inequities in HIV incidence and HIV care is *Impact Triad* in Guilford County, North Carolina. *Impact Triad* uses community-based peer navigation to provide young gay, bisexual, and other MSM as well as transgender women of color with information on HIV prevention and treatment, education access, and employment opportunities (Mann-Jackson et al., 2021). Peer navigators also utilize social media to build social support and program staff receive anti-discrimination training to reduce participant experiences of discrimination (Mann-Jackson et al., 2021). Both these interventions, however, focused on overcoming structural barriers mostly at the individual-level and targeted LGBTQIA+ communities—different strategies may be needed for PWID/LWH. More longitudinal or intervention studies to examine potential causal pathways between social determinants and HIV care outcomes are needed to assess if targeting these factors are effective

in improving health outcomes among PWID/LWH. In addition, interventions addressing structural factors at higher levels (e.g., community or system) are needed to ultimately effect change.

An unexpected result of this study was that ever-injecting drugs was not associated with syndemic burden. Previous studies have found substance use is strongly associated with other syndemic factors, such as depression, and reduced HIV care. For instance, a study on the syndemic effects of substance use, depression, education, and ethnicity on HIV care found that while alcohol dependence alone was not a significant predictor for HIV care retention, the interaction of alcohol use disorder and depression was significantly associated with lower HIV care retention (Myers et al., 2021). Another study on Black and Hispanic/Latinx PLWH found ever or recently injecting drugs was associated with sustained ART adherence, which the authors contributed to the length of time since diagnosis and experience managing ART. Participants indicated in interviews that while substance use along with its associated stigma and poor mental health were barriers to sustained ART adherence, finding social support and establishing emotional and material stability were ways to overcome them (Gwadz et al., 2021).

Factors such as social support and resiliency may therefore be an explanation for the statistical non-significance of ever IDU in the current study. Other studies support an association between strong social, spiritual, or religious support and abstaining from drug use, better mental health, and improved ART adherence (Avants et al., 2001; Durvasula & Miller, 2014; McMahon et al., 2019; Préau et al., 2007). Notably, these studies were all conducted among persons in recovery from substance use disorders. Of the 247 participants in this study reporting ever-injecting drugs, 79.3% did not indicate they had injected in the past 12 months. Therefore, the results may show resiliency associated with being in recovery reduces burden associated with

IDU. More research is needed on the effects of factors associated with recovery (e.g., social support and resiliency) on syndemic burden and HIV care and coverage to assess if interventions which include social support and strategies for resilience could improve outcomes among PWID/LWH.

This study assessed a model of syndemic burden based on theory and the existing literature; however, there may be additional factors which influence syndemic burden not included in this study. For instance, stigma related to HIV is likely not the only type of stigma PLWH experience. Drug use, like HIV, is highly stigmatized. People who use drugs experience discrimination, alienation, and perceive being devalued by others (Ahern et al., 2007). This stigmatization is the result of many factors, including social norms, stereotypes of those addicted to drugs, and the criminalization of drug use (Ahern et al., 2007; Biancarelli et al., 2019; Hatzenbuehler, 2018). Therefore, for PWID/LWH, the presence of both HIV and drug use stigmas, along with other identity-based stigmas (e.g., gender, race/ethnicity, homelessness, etc.), can create a complex interaction known as intersectional stigma. While the intersection of these stigmas is not additive, those with multiple stigmas tend to have higher overall stigma levels and poorer mental health than those with fewer stigmas (Calabrese et al., 2016; Do et al., 2021; Logie et al., 2013; Rudolph et al., 2012). Intersectional stigma can result in poorer health outcomes than when one stigma is experienced alone. For instance, PWID/LWH who feel discrimination based on their HIV or drug use status may withhold information from providers or avoid seeing them at all (Gwadz et al., 2016, 2021; Koester et al., 2019). Further, these intersecting stigmas have been identified by multiple studies as a barrier to ART adherence (Gwadz et al., 2016, 2021; Katz et al., 2013; Shrestha et al., 2019).

In this study, those currently or ever injecting drugs reported lower average HIV stigma scores than those who had never injected drugs. While the reason behind this difference is unclear, I hypothesize PWID/LWH may build resilience due to coping with intersecting stigmas or through the process of being in recovery. Another possibility is that participants deem other stigmas, such as stigma associated with drug use, as "worse" than HIV stigma. Future research should investigate how these intersecting stigmas are experienced by PWID/LWH and ultimately their effect on syndemic burden and HIV care outcomes.

In addition to other factors potentially influencing syndemic burden, there are likely other valid models or theories for the relationships between drug use, HIV stigma, mental health, and HIV care and coverage. However, the results of this study support the inclusion of mental health care and stigma reduction into interventions which aim to decrease syndemic burden and increase HIV care and coverage. Further, this study raised important future directions for research among PWID/LWH, including more robust, longitudinal studies to better understand the effects of recovery on syndemic burden and HIV care and coverage in this population. For instance, expanding MMP to all states or creating a longitudinal cohort for MMP would provide more robust data to inform interventions and policies needed to address syndemic burden. Further, more research is needed on the effects of intersecting stigmas among PWID/LWH. Including additional stigma measures (e.g., for drug use, gender, sexual orientation, etc.) in diverse national surveys, such as MMP, would help raise awareness of the issue and help us better understand this phenomenon. Improving our understanding of recovery from substance dependence and the intersecting stigmas of HIV and drug use will refine our targets for intervention and ultimately improve the overall health of PWID/LWH.

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APPENDIX A: LIST OF ABBREVIATIONS

Adh.	Adherence
AHR	Adjusted hazard ratio
AIDS	Acquired immunodeficiency syndrome
AIR	Adjusted incidence rate ratio
ALIVE	AIDS Linked to the Intravenous Experience
AOR	Adjusted odds ratio
APA	American Psychological Association
Appt.	Appointment
aRH	Adjusted relative hazard
ART	Antiretroviral therapy
BEACON	Being Active and Connected study
CDC	Centers for Disease Control and Prevention
CES-D	Center for Epidemiologic Studies Depression Scale
CFA	Confirmatory factor analysis
CFI	Comparative fit index
CGI	Clinical Global Impression score
CI	Confidence interval
DHHS	Department of Health and Human Services
DSM	Diagnostic and Statistical Manual of Mental Disorders
e	Error term
EHE	Ending the HIV Epidemic
GAD	General Anxiety Disorder
GED	General Education Diploma
HAART	Highly-active antiretroviral therapy
HIV	Human immunodeficiency virus
HRQOL	Health-related quality of life
HS	High school
IDU	Intravenous drug use
Ins.	Insurance
INSPIRE	Intervention for Seropositive Injection Drug Users - Research and Evaluation study
IRB	Institutional Review Board
JHHCC	Johns Hopkins HIV Clinical Cohort
MANCOVA	Multivariate analysis of covariance
MLR	Maximum likelihood estimation with robust standard errors
MMP	Medical Monitoring Project
MSM	Men who have sex with men
NCS	National Comorbidity Survey

NH	Non-Hispanic
NHSS	National HIV Surveillance System
OCD	Obsessive compulsive disorder
OR	Odds ratio
PHQ	Patient Health Questionnaire
PLWH	People living with HIV
PTSD	Post-traumatic stress disorder
PWEID	People who have ever injected drugs
PWID	People who inject drugs
PWID/LWH	People who inject drugs and are living with HIV
Ref.	Referent category
RI	Referent indicator
RMSEA	Root mean square error of approximation
RR	Relative risk
SAVA	Substance Abuse, Violence, and AIDS
SE	Standard error
SEM	Structural equation model
SRMR	Standard root mean square residual
STI	Sexually transmitted infection
SUMIC	Substance Use, Mental Illness, and Familial Conflict Non-Negotiation
TLC	TransLife Care
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNCG	University of North Carolina Greensboro
US	United States
WIHS	Women's Interagency HIV Study

APPENDIX B: UNCG IRB DETERMINATION

OFFICE OF RESEARCH INTEGRITY
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To: Rachel Faller
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From: UNCG IRB

Date: 11/03/2020

RE: Determination that Research or Research-Like Activity does not require IRB Approval
Study #: 21-0158

Study Title: Associations between Mental Health and the HIV Care Continuum in People Who Inject Drugs

This submission was reviewed by the above-referenced IRB. The IRB has determined that this submission does not constitute human subjects research as defined under federal regulations [45 CFR 46.102 (d or f)] and does not require IRB approval.

Study Description:

This study will use secondary data from CDC's Medical Monitoring Project to examine the relationships between depression and anxiety, intravenous drug use, and the HIV care continuum. We will examine how mental health and drug use (both recent and lifetime) are associated with HIV care engagement, antiretroviral therapy adherence, and viral suppression.

- If your study protocol changes in such a way that this determination will no longer apply, you should contact the above IRB before making the changes.